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Reversal of Stereoselectivity in Cycloadditions of Five-Membered Cyclic Nitrones Derived from Hexoses

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Abstract: Two five-membered cyclic nitrones derived from hexoses, a newly synthesized D-*allo*-configured nitrone and an already known D-*talo*-configured nitrone, have been examined in 1,3-dipolar cycloaddition reactions with vinyl acetate, allyl benzoate, methyl acrylate, acrylonitrile, and vinylene carbonate. The reactions of the D-*allo*-configured nitrone proceeded preferentially through the expected *exo-anti* transition state, but all the cycloadditions of the D-*talo*-configured nitrone surprisingly showed high *exo-syn* selectivity. This reversal of stereoselectivity has been explained by 3D analysis of the preferred conformations of the nitrones, obtained from X-ray data. The structures were further inspected using CONFLEX, PM5, and DFT calculations. All these methods revealed that the dioxolane substituents attached to C-5 of both nitrones had opposite spatial locations.

Introduction

The preparation of five-membered cyclic nitrones from pentoses[1] is a subject of great interest. These compounds are often used in the synthesis of polyhydroxylated pyrrolizidine alkaloids.[2] Many of them have been used in stereoselective 1,3-dipolar cycloaddition reactions to form chiral bicyclic pyrroloisoxazolidines, valuable intermediates for the preparation of many biologically active natural products and their analogues.[3] Conversely, a similar class of cyclic nitrones derived from hexoses have not been explored in detail to date;[4] the highly *anti*-stereoselective nucleophilic additions that have been reported for the D-*talo*-configured nitrone **1** derived from D-mannose are an exception (Figure 1).[5,6] Recently, we were the first to report the stereoselective 1,3-dipolar cycloaddition of nitrone **1** with vinyl acetate (**2**; Scheme 1).[7] Interestingly, the reaction unexpectedly proceeded preferentially through an *exo-syn* transition state to give a mixture of two isomeric isoxazolidines **3a** and **3b** in a 13:87 ratio as single regioisomers (the *syn*/*anti* nomenclature refers to the attack of the dipolarophile with respect to the vicinal OR group of the nitrone).[2a] The major *syn* isomer **3b** was subsequently transformed into a hydroxymethylated pyrrolizidine derivative with the same relative configuration at C-1, C-2, C-3, C-5, and C-7a as, for instance, the naturally occurring hyacinthacines B_2, C_2, and C_3 (Scheme 1, Figure 1).

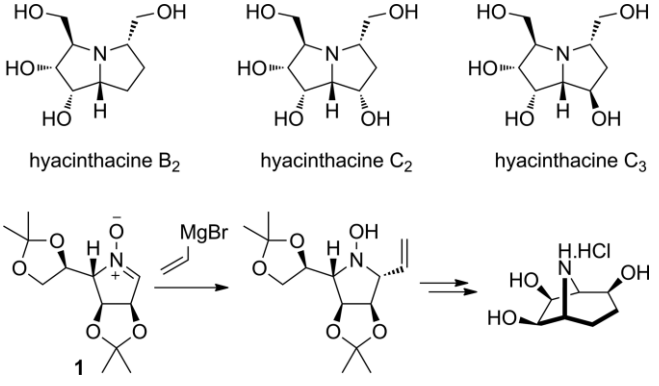

Figure 1. Polyhydroxylated pyrrolizidine alkaloids and a calystegine analogue.

With the aim of synthesizing pyrrolizidines structurally related to the alkaloids mentioned above, we synthesized a new D-*allo*-configured nitrone **4** (Figure 2). Surprisingly, the 1,3-dipolar cycloaddition of this compound with vinyl acetate (**2**) took place with *anti* selectivity, opposite to that obtained with nitrone **1**. The observation of these different selectivities prompted us to further examine the stereochemical behaviour of nitrones **1** and **4**. In this paper, we report the results of their 1,3-dipolar cycloadditions with five representative dipolarophiles, namely vinyl acetate (**2**), allyl benzoate (**5**), methyl acrylate (**6**), acrylonitrile (**7**), and vinylene carbonate (**8**) (Figure 2).

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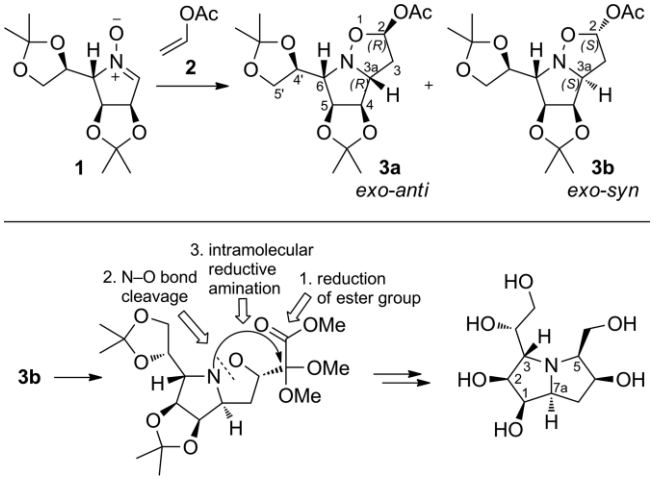


Scheme 1. *syn*-Stereoselective 1,3-dipolar cycloaddition of nitrone **1** with vinyl acetate (**2**). Reaction conditions: vinyl acetate, 75 °C, 24 h, 92 %, **3a**/**3b**, 13:87. Strategy for the synthesis of a hydroxymethylated pyrrolizidine derivative.

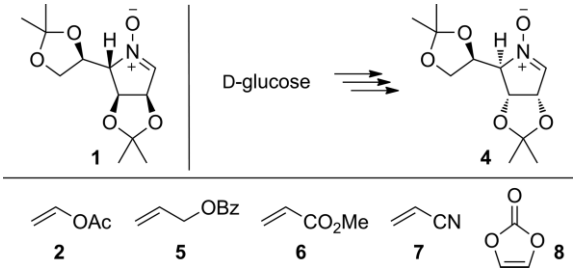
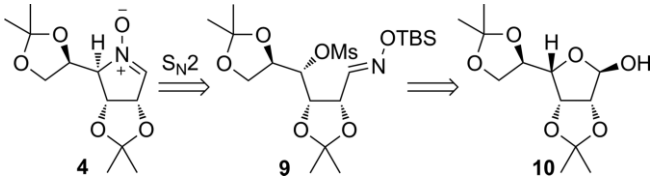


Figure 2. D-Mannose-derived nitrone **1**, D-glucose-derived nitrone **4**, and representative dipolarophiles **2** and **5**–**8**.

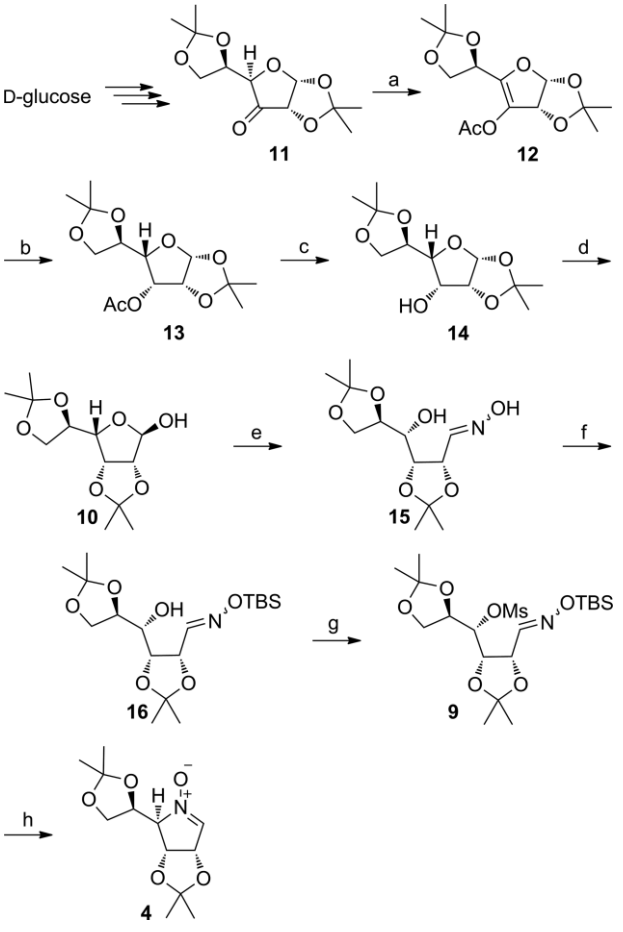
Results and Discussion

Known nitrone **1** was readily prepared from D-mannose by Tamura's protocol.[5] The new D-*allo*-configured nitrone **4** was synthesized similarly starting from D-glucose, using an intramolecular S_N2 reaction of D-gulose oxime **9** obtained from D-gulofuranose **10** as a key step (Scheme 2).



Scheme 2. Retrosynthetic analysis of D-*allo*-configured nitrone **4**.

As outlined in Scheme 3, D-glucose was initially transformed into 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose (**11**) by a two-step procedure consisting of the formation of 1,2:5,6-di-*O*-isopropylidene-D-glucose, followed by oxidation of the unprotected hydroxy group with PDC (pyridinium dichromate).[8] Reaction of 3-keto derivative **11** with acetic anhydride under basic conditions provided enol acetate **12** in 69 % yield.[9] Subsequent *cis*-stereoselective hydrogenation of this compound gave gulose derivative **13** exclusively in 79 % yield.[10] Treatment of compound **13** with sodium methoxide produced 1,2:5,6-di-*O*-isopropylidene-α-D-gulofuranose (**14**) in 89 % yield.[9b] Isomerization of 1,2:5,6-bis(acetonide) **14** with *p*-toluenesulfonic acid monohydrate (PTSA·H_2O) in acetone then gave the thermodynamically more stable 2,3:5,6-di-*O*-isopropylidene-β-D-gulofuranose (**10**) in 83 % yield. Condensation of this compound with hydroxylamine hydrochloride produced oxime **15** in 88 % yield as an inseparable mixture of (*E*) and (*Z*) isomers in a ratio of 60:40.[11] Compound **15** was then subjected to reaction with *tert*-butyldimethylchlorosilane (TBSCl), and silylated oxime **16** was formed selectively in 99 % yield [(*E*)/(*Z*) ≈ 60:40]. Treatment of **16** with methanesulfonyl chloride (MsCl) gave oxime **9** bearing a leaving group at C-4. Unfortunately, one-pot TBAF-mediated desilylation (TBAF = tetra-*n*-butylammonium fluoride) and spontaneous ring-closure did not give nitrone **4** in satisfactory yield and purity. To solve this problem, oxime **9** was conveniently desilylated, then the THF was replaced by a methanol/water mixture, and the cyclization was completed by adding a large excess of hydroxylamine hydrochloride/sodium hydrogen carbonate, followed by heating.[12]



Scheme 3. Synthesis of nitrone **4**. Reaction conditions: (a) acetic anhydride, pyridine, 60 °C, 6 h, 69 %; (b) H_2 (20 psi), Pd/C, ethanol, room temp., 6 h, 79 %; (c) sodium methoxide, methanol, room temp., 30 min, 89 %; (d) PTSA·H_2O, acetone, room temp., 4 h, 83 %; (e) NH_2OH·HCl, $NaHCO_3$, ethanol/water (1:1), room temp., 12 h, 88 %, (*E*)/(*Z*) = 60:40; (f) TBSCl in toluene, imidazole, CH_2Cl_2, room temp., 3 h, 99 %, (*E*)/(*Z*) = 60:40; (g) MsCl, Et_3N, DMAP [4-(dimethylamino)pyridine], CH_2Cl_2, 0 °C to room temp., 12 h, 84 %, (*E*)/(*Z*) = 55:45; (h) (i) TBAF, anhydrous THF, 0 °C, 30 min; (ii) NH_2OH·HCl, $NaHCO_3$, methanol/water (4:1), reflux, 12 h, 81 % over two steps.

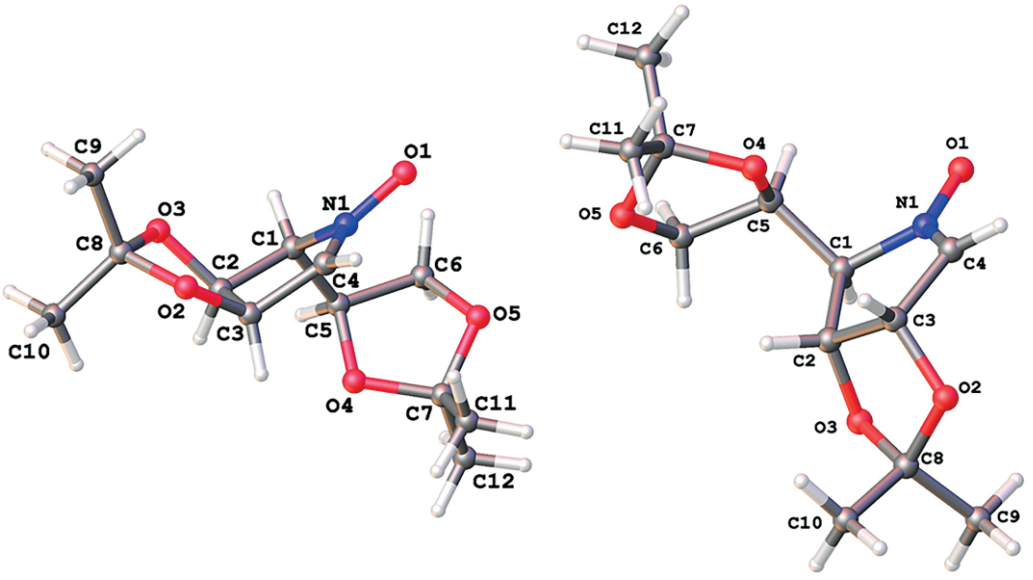
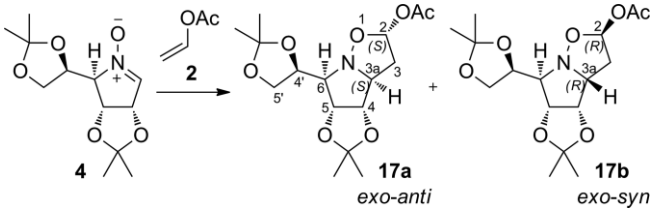


Figure 3. Molecular structures of D-*talo*-configured nitrone **1** (left) and D-*allo*-configured nitrone **4** (right), confirmed by X-ray crystallographic analysis.

Finally, the salts were removed by extraction, and nitrone **4** was isolated by flash column chromatography (FCC) in 81 % yield over two steps. Its structure was assigned on the basis of ^{1}H and ^{13}C NMR spectroscopy (see the Supporting Information). The absolute configurations of both nitrones **1** and **4** were verified by X-ray crystallographic analysis (Figure 3).

With nitrone **4** in hand, we immediately attempted its 1,3-dipolar cycloaddition with vinyl acetate (**2**). The reaction was carried out at 75 °C for 24 h (Scheme 4). Two diastereomeric isoxazolidines **17a** and **17b** were formed in a **17a**/**17b** ratio of 70:30, and were isolated in 88 % total yield after purification by FCC. Both cycloadducts were characterized by NMR spectroscopy.



Scheme 4. *anti*-Stereoselective 1,3-dipolar cycloaddition of nitrone **4** with vinyl acetate (**2**). Reaction conditions: vinyl acetate, 75 °C, 24 h, 88 %, **17a**/**17b** (70:30).

The relative configurations of **17a** and **17b** were assigned as major *exo-anti* diastereoisomer **17a** and minor *exo-syn* cycloadduct **17b** based on the results of NOESY 1D experiments as follows (Figure 4). For **17a**, irradiation of proton 3a-H resulted in enhancement of the signal corresponding to 3^{a}-H (3.7 %), whereas a weaker NOE was observed for the protons 3^{b}-H (0.9 %) and 4-H (0.5 %). On the other hand, when 3^{b}-H was irradiated, a significant NOE was observed for the protons 2-H (3.3 %) and 4-H (3.8 %). The relative configuration of **17b** was determined based in particular on the existence of NOE enhancements between 3a-H and the protons 4-H (2.5 %) and 3^{a}-H (3.5 %). The irradiation of proton 3^{a}-H also resulted in a small enhancement of the proton 2-H signal (1.1 %). A strong NOE was observed between the protons 2-H and 3^{b}-H (2.7 %).

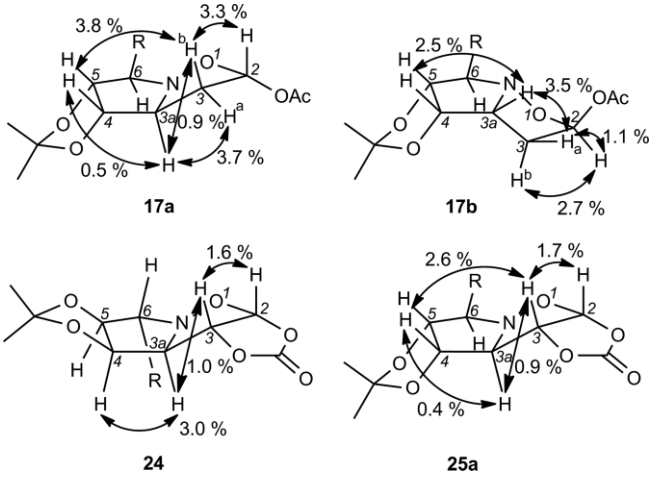
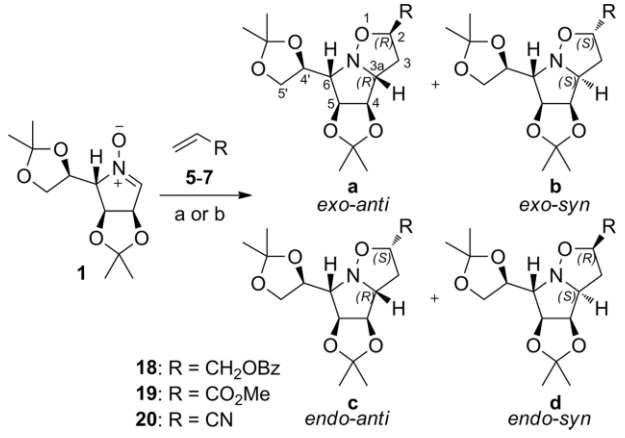


Figure 4. Selected NOE enhancements observed in isoxazolidines **17a**, **17b**, **24**, and **25a**. Arrows show the NOESY correlations.

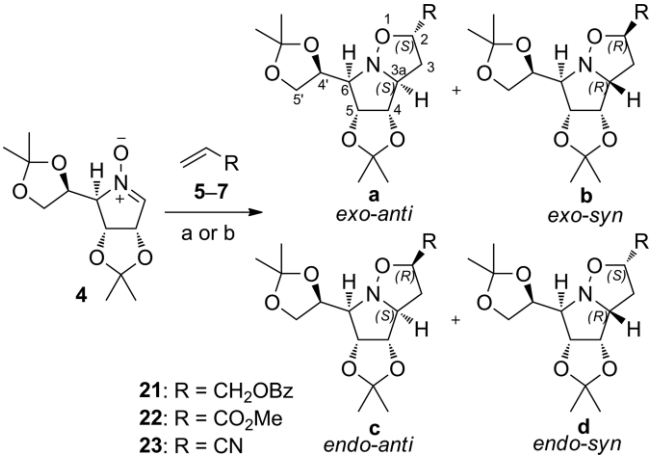
Indeed, the cycloaddition of nitrone **4** proceeded regioselectively and preferentially through an *exo-anti* transition state. This is fully consistent with the statement that the stereochemical outcome of the cycloaddition is controlled by the C-3 stereocentre of the five-membered nitrone.[2a] As described in the introduction, the observed *anti* selectivity was in strong contrast with the *syn* selectivity observed for the cycloaddition of nitrone **1** with vinyl acetate (**2**; Scheme 1). Encouraged by these different stereochemical outcomes depending on the nitrone used, both nitrones **1** and **4** were briefly examined in cycloaddition reactions with allyl benzoate (**5**), methyl acrylate (**6**), and acrylonitrile (**7**) (Schemes 5 and 6). All the reactions were carried out in toluene at 80 °C for 24 or 48 h. When the reactions were complete, the solvent was simply evaporated in vacuo, and the products were purified by FCC followed by

preparative TLC if needed. All the cycloadducts that were isolated as single compounds were characterized by ^{1}H and ^{13}C NMR spectroscopy, including NOESY 1D experiments (see the Supporting Information).



Scheme 5. 1,3-Dipolar cycloadditions of nitrone **1** with dipolarophiles **5**–**7**. Reaction conditions: (a) toluene, 80 °C, 48 h; (b) toluene, 80 °C, 24 h.

To determine the relative configurations of the cycloadducts, we mainly considered decisive enhancements between the protons 3a-H/4-H and 2-H/3-H/3a-H (see the Supporting Information). More specifically, a greater enhancement of the 4-H proton signal (2.2–3.5 %) upon irradiation of the 3a-H proton signal unambiguously indicated a 3a,4-*syn* configuration (this was seen for all *syn*-**b** and *syn*-**d** isomers). A significantly smaller enhancement of the 4-H proton signal (0.2–0.5 %) implied a 3a,4-*anti* configuration (this was observed for all *anti*-**a** and *anti*-**c** isomers). For the *exo*-**a** and *exo*-**b** isomers, when the 3^{b}-H proton was irradiated, along with a strong NOE for the 2-H proton (2.1–3.4 %), a weak NOE was observed for the 3a-H proton (0.3–1.1 %). On the other hand, the irradiation of the 3^{a}-H proton resulted in a strong enhancement of the signal corresponding to 3a-H (2.1–4.2 %). All *endo*-**d** isomers (**18**–**20**) were characterized by a higher NOE between 3^{b}-H and 3a-H protons (1.4–2.5 %), whereas a smaller enhancement of 3a-H proton signal was observed upon irradiation of 3^{a}-H (0.5–1.3 %).



Scheme 6. 1,3-Dipolar cycloadditions of nitrone **4** with dipolarophiles **5**–**7**. Reaction conditions: (a) toluene, 80 °C, 48 h; (b) toluene, 80 °C, 24 h.

With a view to confirming the configuration of the major isomers of both series as assigned by NMR spectroscopy, the best-crystallizing isoxazolidines **18b** and **21a** were subjected to X-ray crystallographic analysis. The data obtained verified the expected absolute configurations (Figure 5).

The results obtained demonstrate that nitrone **1** again reacted highly regio- and stereoselectively in favour of *exo*-*syn* cycloadducts **18b**–**20b** (Scheme 5, Table 1). The *exo*-*anti* diastereoisomers **18a**–**20a** were formed as minor components. Surprisingly, considerable amounts of an unexpected cycloadduct (**d**) derived from an *endo*-*syn* approach were isolated in satisfactory yields and purities (see the Supporting Information). The *syn*/*anti* ratios varied from 80:20 to 85:15, and were almost identical with those resulting from cycloaddition with vinyl acetate (**2**). On the other hand, 1,3-dipolar cycloadditions

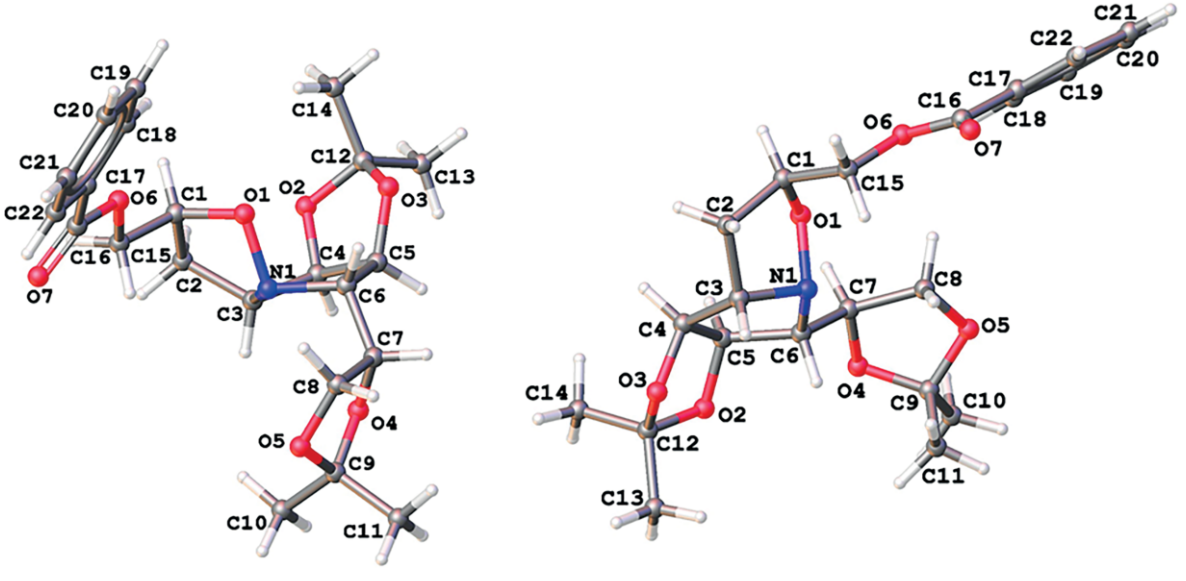


Figure 5. Molecular structures of the major cycloadducts **18b** (left) and **21a** (right), confirmed by X-ray crystallographic analysis.

of nitrone **4** proceeded preferentially through an *exo* approach of the dipolarophile *anti* to the vicinal substituent of the nitrone to form major *exo-anti* cycloadducts **21a**–**23a** (Scheme 6, Table 2). Reaction with acrylonitrile (**7**) gave a significant yield of *endo-anti* diastereoisomer **23c**. A third cycloadduct, also assumed to be an *endo-anti* isomer, was detected by NMR spectroscopy in the cycloaddition with methyl acrylate (**6**), but it was not possible to isolate and characterize it.

Table 1. 1,3-Dipolar cycloadditions of nitrone **1** with dipolarophiles **5**–**7**.

Entry	Product	R	Yield [%][a]	Ratio **a**/**b**/**c**/**d**[b]
1	**18**	CH_2OBz	75	15:70:–:15
2	**19**	CO_2Me	90	15:50:–:35
3	**20**	CN	79	20:55:–:25

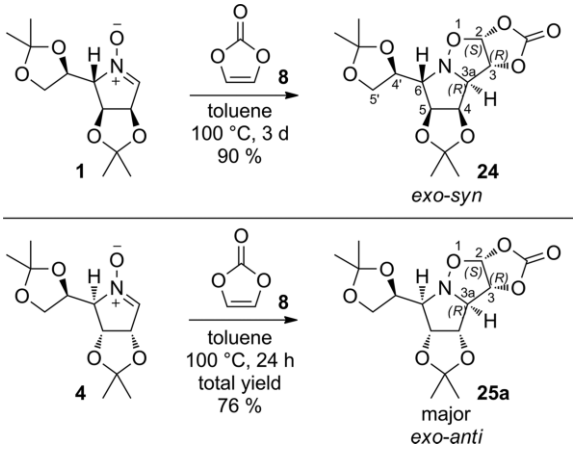
[a] Total yield of the reaction. [b] Diastereomeric ratios were determined from the ^1H NMR spectra of the crude product.

Table 2. 1,3-Dipolar cycloadditions of nitrone **4** with dipolarophiles **5**–**7**.

Entry	Product	R	Yield [%][a]	Ratio **a**/**b**/**c**/**d**[b]
1	**21**	CH_2OBz	81	75:25:–:–
2	**22**	CO_2Me	96	75:25:–:–[c]
3	**23**	CN	78	65:15:20:–[d]

[a] Total yield of the reaction. [b] Diastereomeric ratios were determined from the ^1H NMR spectra of the crude product mixture. [c] A third cycloadduct was detected by NMR spectroscopy, but it was not possible to isolate and characterize it. [d] Traces of a fourth cycloadduct were detected by NMR spectroscopy.

As a part of our interest in hydroxylated isoxazolidines,[13] nitrones **1** and **4** were also examined in 1,3-dipolar cycloaddition reactions with vinylene carbonate (**8**), which gave C-3-*O*-functionalized isoxazolidines **24** and **25** (Scheme 7).



Scheme 7. 1,3-Dipolar cycloadditions of nitrone **1** and nitrone **4** with vinylene carbonate (**8**).

Both reactions showed high diastereoselectivities, but once again these were opposite in sense. Similarly, as described previously, the cycloaddition of nitrone **1** led to *exo-syn* isoxazolidine **24** as a single product in 90 % yield. The reaction of nitrone **4** led preferentially to *exo-anti* isoxazolidine **25a**, formed together with minor *exo-syn* isomer **25b** in 76 % total yield (*syn*/*anti* = 10:90). The structures of **24**, **25a** and **25b** were assigned based on NMR spectroscopy (see the Supporting Information), including NOESY 1D experiments (Figure 4).

It can be summarized that the cycloadditions of nitrone **1**, derived from D-mannose, led to *exo-syn* cycloadducts as the major products, whereas nitrone **4**, derived from D-glucose, reacted with *exo-anti* selectivity. We assume that such a stereochemical contradiction arises from the steric influence of the dioxolane substituent attached at C-5 of the nitrone.

To explain and clarify this phenomenon, let us consider the possible approaches of the dipolarophile to nitrones **1** and **4**, as illustrated in Figures 6 and 7. Primarily, it is necessary to note that the two nitrones under comparison differ in how the above-mentioned bulky substituent is arranged. Looking at preferred minimum-energy conformations based on detailed X-ray crystallographic analysis (Figure 3), it is easy to see which face of each of the two nitrones will be attacked preferentially. In nitrone **1**, the dioxolane ring is almost completely bent under the pyrroline moiety (Figure 6), whereas in nitrone **4** it is considerably twisted away from this area (Figure 7). As a consequence, the bottom side of nitrone **1** is sterically more hindered than its top side. Because of this steric hindrance, cycloadditions predominantly proceed through an *exo-syn* transition state, leading to the formation of 3a,4-*syn*-2,3a-*trans*-isoxazolidines as the major isomers (for example **18b**; Figure 5). Conversely, bottom-side attack on nitrone **4**, which would also deliver *syn* diastereoisomers, is disfavoured because of the obvious steric repulsions between the dipolarophile and the isopropylidenedioxy substructure located at C-3 and C-4. In this case, the top side of nitrone **4** is more accessible, despite the large dioxolane substituent at C-5, and the cycloadditions proceed with good *anti* selectivity to give mainly 3a,4-*anti*-2,3a-*trans*-isoxazolidines as usual (for example **21a**; Figure 5). The results obtained with the sterically demanding vinylene carbonate (**8**) confirm what has been just stated. We suppose that the improved diastereoselectivities in favour of the *exo-syn* isomer for nitrone **1** and *exo-anti* isomer in the case of nitrone **4** are due to the increased steric demand of the dipolarophile.

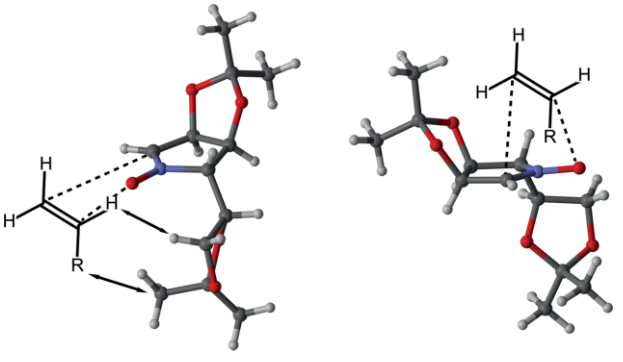


Figure 6. Preferred conformation of D-*talo*-configured nitrone **1** resulting from its X-ray structure inspected by CONFLEX calculations, and possible approaches of the dipolarophile; *anti* approach (left) and *syn* approach (right).

Concerning *exo*/*endo* selectivity, when the less bulky acrylonitrile (**7**) was used, the *endo* adducts were also formed in noticeable amounts. The same was observed when methyl acrylate (**6**) was used. The cycloaddition reactions with the more hindered allyl benzoate (**5**) gave the *exo* products as the major

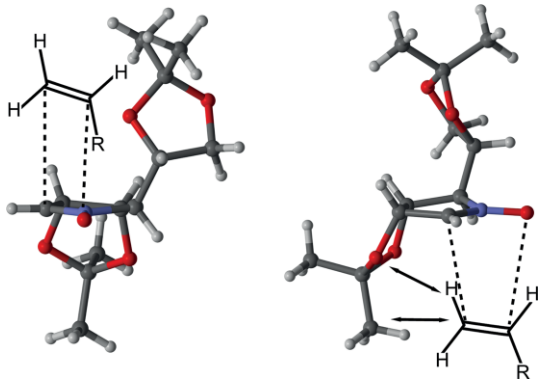


Figure 7. Preferred conformation of D-*allo*-configured nitrone **4** resulting from its X-ray structure inspected by CONFLEX calculations, and possible approaches of the dipolarophile; *anti* approach (left) and *syn* approach (right).

or exclusive products. With vinyl acetate (**2**) and vinylene carbonate (**8**), a 1,2-disubstituted alkene, the diastereoselectivity was completely in favour of the *exo* cycloadducts. Finally, the *endo-anti* approach to nitrone **1** and the *endo-syn* approach to nitrone **4** are strongly disfavoured by repulsive interactions between the dipolarophile and the substituents on the nitrone ring.

As all these speculations are based on X-ray geometries, i.e., rigid crystal-lattice packed conformations, we also inspected these geometries using CONFLEX,[14a] PM5,[14b] and low-level DFT[14c] based geometry optimizations. All the minimum-energy geometries obtained from those calculations were similar to the X-ray geometries discussed above in terms of the spatial orientation of the bulky isopropylidenedioxy unit and other key features (see the Supporting Information).

Conclusions

We have prepared a new D-*allo*-configured five-membered cyclic nitrone starting from D-glucose as a counterpart of the already known D-*talo*-configured nitrone derived from D-mannose. Both nitrones were examined in cycloaddition reactions with vinyl acetate, allyl benzoate, methyl acrylate, acrylonitrile, and vinylene carbonate. In all cases, the reactions of the D-*talo*-configured nitrone surprisingly led to *exo-syn* cycloadducts as the major products, whereas the D-*allo*-configured nitrone reacted with *exo-anti* selectivity. This reversal of stereoselectivity has been explained by 3D analysis of preferred conformations of nitrones, obtained from X-ray data. The structures were further inspected using CONFLEX, PM5, and DFT calculations. All these methods show that the dioxolane substituents attached to C-5 of both the nitrones have opposite spatial locations, even though they are attached to the nitrone ring with the same relative configuration.

Experimental Section

General Remarks: Melting points were measured with a Melting Point B-540 apparatus (Büchi). HRMS analysis was carried out with an Orbittrap Velos Pro spectrometer (Thermo Fisher Scientific). MS analysis was carried out with an Agilent 1260B LC–MS system with a multimode ion source (ESI + APCI) in positive mode, 50 % scan and 50 % SIM (selected-ion monitoring). Infrared (IR) spectra were recorded with a Nicolet 5700 FTIR spectrometer with an ATR Smart Orbit Diamond adapter (Thermo Electron Corporation), and data are reported as wavenumbers (cm^{-1}). NMR spectra were recorded with a Varian INOVA-300 spectrometer (^1H, 300 MHz, and ^{13}C, 75 MHz) and a Varian V NMR S-600 instrument (^1H, 600 MHz, and ^{13}C, 150 MHz) in $CDCl_3$, using tetramethylsilane as the internal standard. Optical rotations were measured with a JASCO P-2000 polarimeter (concentrations *c* are given in g/100 mL). TLC analysis was carried out using TLC silica gel 60 F_{254} (aluminium sheets, Merck), and plates were visualized with UV light or by treatment with permanganate solution followed by heating. Flash column chromatography (FCC) was carried out with a Büchi system (Pump Manager C-615 and Fraction Collector C-660) using Normasil 60 silica gel (0.040–0.063 mm; VWR). All solvents were dried and distilled according to conventional methods. All reagents were purchased from Sigma–Aldrich, Acros Organics, Alfa Aesar, Merck, or Mikrochem Trade, and were used without further purification.

3-*O*-Acetyl-1,2:5,6-di-*O*-isopropylidene-α-D-erythrohex-3-enose (12): 1,2:5,6-Di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose (**11**; 11 g, 42 mmol), prepared in a two-step procedure from D-glucose,[8] was dissolved in pyridine (24 mL, 30 mmol), and the resulting solution was heated to 60 °C with stirring. Acetic anhydride (12 mL, 13 mmol) was added dropwise, and stirring was continued at 60 °C for 6 h. When TLC showed that the reaction was complete (hexanes/EtOAc, 6:4), the mixture was poured onto crushed ice. Water (50 mL) was added, and the product was extracted with dichloromethane (2 × 40 mL). The combined organic layers were dried with $MgSO_4$, and the solvent was evaporated in vacuo. The residue was purified by FCC (hexanes/EtOAc, 9:1) to give acetate **12** (8.7 g, 29 mmol, 69 %) as a colourless solid. R_f = 0.17 (cyclohexane/EtOAc, 9:1). M.p. 55–56 °C. $[\alpha]_D^{23}$ = –35.1 (*c* = 1.07, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 2991, 2939, 1761, 1373, 1202, 1153, 1099, 1053, 970, 890 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 6.04 (d, *J* = 5.5 Hz, 1 H, 1-H), 5.40 (d, *J* = 5.5 Hz, 1 H, 2-H), 4.71 (pseudo t, *J* = 6.4 Hz, 1 H, 5-H), 4.13–4.02 (m, 2 H, 6^a-H, 6^b-H), 2.22 (s, 3 H, COMe), 1.54 (s, 3 H, Me), 1.48 (s, 3 H, Me), 1.45 (s, 3 H, Me), 1.38 (s, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.9 (C=O), 145.3 (C-4), 129.0 (C-3), 113.5 (CMe_2), 110.4 (CMe_2), 104.0 (C-1), 80.9 (C-2), 68.6 (C-5), 65.9 (C-6), 27.9, 27.8, 25.8, 25.6 (4 CMe_2), 20.5 (CO*Me*) ppm. HRMS (ESI): calcd. for $C_{14}H_{21}O_7$ $[M + H]^+$ 301.1287; found 301.1282.

3-*O*-Acetyl-1,2:5,6-di-*O*-isopropylidene-α-D-gulofuranose (13): 3-*O*-Acetyl-1,2:5,6-di-*O*-isopropylidene-α-D-erythrohex-3-enose (**12**; 8.3 g, 28 mmol) was dissolved in anhydrous ethanol (150 mL). Pd/C (5 wt.-%; 1.7 g) was added, and the mixture was vigorously stirred under hydrogen (20 psi) at room temperature for 6 h. After this time, TLC showed that the reaction was complete (hexanes/EtOAc, 6:4). The catalyst was removed by filtration through a Celite pad, which was then washed with ethanol. The filtrate was concentrated under reduced pressure. The residue was purified by FCC (hexanes/acetone, 9:1) to give acetate **13** (6.7 g, 22 mmol, 79 %) as a colourless solid. R_f = 0.10 (cyclohexane/acetone, 9:1). M.p. 72–74 °C. $[\alpha]_D^{23}$ = +70.1 (*c* = 1.05, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 2989, 2871, 1743, 1375, 1232, 1212, 1117, 1031, 1008, 842 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 5.82 (d, *J* = 4.1 Hz, 1 H, 1-H), 5.08 (dd, *J* = 6.7, 5.7 Hz, 1 H, 3-H), 4.82 (dd, *J* = 5.6, 4.1, 1 H, 2-H), 4.63 (dt, *J* = 9.2, 6.9 Hz, 1 H, 5-H), 4.11 (dd, *J* = 7.3, 5.4 Hz, 1 H, 6^a-H), 4.09 (dd, *J* = 8.1, 5.6 Hz, 1 H, 4-H), 3.54 (dd, *J* = 8.3, 7.4 Hz, 1 H, 6^b-H), 2.14 (s, 3 H, COMe), 1.59 (s, 3 H, Me), 1.45 (s, 3 H, Me), 1.39 (s, 3 H, Me), 1.36 (s, 3 H, Me) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 169.6 (C=O), 114.5 (CMe_2), 109.3 (CMe_2),

105.0 (C-1), 81.3 (C-4), 78.5 (C-2), 75.2 (C-5), 71.8 (C-3), 66.4 (C-6), 26.8 (2 ×), 26.7, 25.3 (4 C*Me*$_2$), 20.6 (CO*Me*) ppm. HRMS (ESI): calcd. for $C_{14}H_{23}O_7$ $[M + H]^+$ 303.1444; found 303.1435.

1,2:5,6-Di-*O*-isopropylidene-α-D-gulofuranose (14): 3-*O*-Acetyl-1,2:5,6-di-*O*-isopropylidene-α-D-gulofuranose (**13**; 6.7 g, 22 mmol) was dissolved in methanol (46 mL). Sodium methoxide (25 wt.-% in methanol; *d* = 0.945 g/mL at 25 °C; 5.1 mL, 22 mmol) was added, and the mixture was stirred at room temperature for 30 min. Then, the solvent was evaporated in vacuo, and water (50 mL) was added to the residue. The mixture was extracted with dichloromethane (3 × 25 mL). The combined organic layers were dried with $MgSO_4$ and concentrated to dryness. The residue was purified by FCC (hexanes/EtOAc, 4:6) to give D-gulofuranose **14** (5.1 g, 19.6 mmol, 89 %) as a colourless solid. R_f = 0.13 (cyclohexane/EtOAc, 6:4). M.p. 103–105 °C. $[\alpha]_D^{23}$ = +30.9 (*c* = 0.98, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 3444, 2991, 2945, 1372, 1215, 1136, 1093, 1023, 838, 819 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.78 (d, *J* = 4.1 Hz, 1 H, 1-H), 4.66 (dd, *J* = 6.3, 4.1 Hz, 1 H, 2-H), 4.48 (dt, *J* = 8.6, 7.0 Hz, 1 H, 5-H), 4.20–4.26 (m, 2 H, 6^a-H, 6^b-H), 3.90 (dd, *J* = 8.6, 5.7 Hz, 1 H, 3-H), 3.72 (dd, *J* = 8.6, 7.2 Hz, 1 H, 4-H), 2.68 (d, *J* = 6.4 Hz, 1 H, OH), 1.63 (s, 3 H, Me), 1.45 (s, 3 H, Me), 1.43 (s, 3 H, Me), 1.38 (s, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 115.0 (C*Me*$_2$), 109.3 (C*Me*$_2$), 105.3 (C-1), 84.3 (C-4), 79.9 (C-2), 75.6 (C-5), 69.7 (C-3), 66.4 (C-6), 27.2, 27.1, 26.7, 25.2 (4 C*Me*$_2$) ppm. HRMS (ESI): calcd. for $C_{12}H_{21}O_6$ $[M + H]^+$ 261.1338; found 261.1333; calcd. for $C_{12}H_{20}O_6Na$ $[M + Na]^+$ 283.1158; found 283.1151.

2,3:5,6-Di-*O*-isopropylidene-β-D-gulofuranose (10): *p*-Toluenesulfonic acid monohydrate (1.9 g, 10 mmol) was added to a solution of 1,2:5,6-di-*O*-isopropylidene-α-D-gulofuranose (**14**; 5.1 g, 20 mmol) in acetone (200 mL). The resulting mixture was stirred at room temperature for 4 h. When TLC showed that the reaction was complete (hexanes/EtOAc, 1:1), a large excess of solid $NaHCO_3$ was added, and stirring was continued for 10 min. Thereafter, the solids were removed by filtration, and the mixture was concentrated under reduced pressure. The residue was purified by FCC (hexanes/EtOAc, 6:4) to give D-gulofuranose **10** (4.3 g, 16.5 mmol, 83 %) as a colourless solid. R_f = 0.29 (cyclohexane/EtOAc, 6:4). M.p. 108–110 °C. $[\alpha]_D^{25}$ = –0.87 (*c* = 1.04, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 3423, 2983, 2918, 1374, 1208, 1057, 1039, 1013, 889, 843 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.46 (d, *J* = 2.3 Hz, 1 H, 1-H), 4.70 (dd, *J* = 5.9, 3.8 Hz, 1 H, 3-H), 4.63 (d, *J* = 5.9 Hz, 1 H, 2-H), 4.37 (dt, *J* = 8.4, 7.1 Hz, 1 H, 5-H), 4.22 (dd, *J* = 8.4, 6.5 Hz, 1 H, 6^a-H), 4.14 (dd, *J* = 8.4, 3.7 Hz, 1 H, 4-H), 3.73 (dd, *J* = 8.3, 7.3 Hz, 1 H, 6^b-H), 2.84 (br. s, 1 H, OH), 1.45 (s, 6 H, 2 Me), 1.39 (s, 3 H, Me), 1.29 (s, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 112.9 (C*Me*$_2$), 109.8 (C*Me*$_2$), 101.4 (C-1), 85.7 (C-4), 82.3 (C-2), 79.9 (C-3), 75.5 (C-5), 66.0 (C-6), 26.7, 26.0, 25.4, 24.7 (4 C*Me*$_2$) ppm. HRMS (ESI): calcd. for $C_{12}H_{21}O_6$ $[M + H]^+$ 261.1338; found 261.1331; calcd. for $C_{12}H_{20}O_6Na$ $[M + Na]^+$ 283.1158; found 283.1149.

(*E*,*Z*)-2,3:5,6-Di-*O*-isopropylidene-D-gulose Oxime (15): Hydroxylamine hydrochloride (5.3 g, 76 mmol) was dissolved in a mixture of ethanol and water (1:1, v/v; 80 mL). Solid $NaHCO_3$ (5.5 g, 66 mmol) was added, followed by β-D-gulofuranose **10** (4.3 g, 16.5 mmol). The resulting mixture was vigorously stirred at room temperature for 12 h. When TLC showed that the starting furanose had disappeared (dichloromethane/methanol, 95:5), the ethanol was partially evaporated under reduced pressure, and then brine (80 mL) was added. The product was extracted with ethyl acetate (4 × 50 mL). The combined organic layers were dried with $MgSO_4$, and the solvent was evaporated in vacuo. The residue was purified by FCC (dichloromethane/methanol, 97:3) to give an inseparable (*E*)/(*Z*) mixture of **15** [4.0 g, 14.5 mmol, 88 %, (*E*)/(*Z*) ≈ 60:40] as a colourless oil. R_f(*E*,*Z*) = 0.30 (dichloromethane/methanol, 95:5). ^1H NMR (600 MHz, $CDCl_3$): δ = 9.52 (br. s, 0.6 H, OH), 9.12 (br. s, 0.4 H, OH), 7.57 (d, *J* = 8.0 Hz, 0.4 H, 1-H), 7.12 (d, *J* = 4.0 Hz, 0.6 H, 1-H), 5.29 (dd, *J* = 7.5, 4.0 Hz, 0.6 H, 2-H), 4.75 (dd, *J* = 7.8, 7.1 Hz, 0.4 H, 2-H), 4.34 (d, *J* = 7.7 Hz, 0.6 H, 3-H), 4.28–4.23 (m, 1 H, 5-H$_E$, 3-H$_Z$), 4.21 (dt, *J* = 6.7, 5.1 Hz, 0.4 H, 5-H), 4.11 (dd, *J* = 8.0, 6.6 Hz, 0.6 H, 6^a-H), 4.05 (dd, *J* = 8.3, 6.6 Hz, 0.4 H, 6^a-H), 3.85 (dd, *J* = 8.2, 6.9 Hz, 0.4 H, 6^b-H), 3.77 (d, *J* = 5.8 Hz, 0.6 H, OH), 3.66 (pseudo t, *J* = 7.9 Hz, 0.6 H, 6^b-H), 3.63–3.60 (m, 0.4 H, 4-H), 3.44–3.41 (m, 0.6 H, 4-H), 2.67 (br. s, 0.4 H, OH), 1.56 (s, 1.8 H, Me), 1.55 (s, 1.2 H, Me), 1.45 (s, 1.2 H, Me), 1.43 (s, 1.8 H, Me), 1.39 (s, 3 H, Me), 1.38 (s, 1.2 H, Me), 1.37 (s, 1.8 H, Me) ppm. ^{13}C NMR [data for the major (*E*) isomer, extracted from the spectrum of the mixture; 150 MHz, $CDCl_3$]: δ = 151.9 (C-1), 110.0, 109.7 (2 C*Me*$_2$), 78.1 (C-5), 77.8 (C-3), 72.5 (C-2), 70.7 (C-4), 66.2 (C-6), 26.5, 26.2, 25.4, 24.6 (4 C*Me*$_2$) ppm. ^{13}C NMR [data for the minor (*Z*) isomer, extracted from the spectrum of the mixture; 150 MHz, $CDCl_3$]: δ = 149.4 (C-1), 110.2, 109.8 (2 C*Me*$_2$), 77.9 (C-3), 76.4 (C-5), 75.1 (C-2), 69.2 (C-4), 65.8 (C-6), 27.1, 26.4, 25.3, 25.1 (4 C*Me*$_2$) ppm. MS (ESI + APCI): *m*/*z* = 276.2 ($C_{12}H_{22}NO_6$) $[M + H]^+$.

(*E*,*Z*)-2,3:5,6-Di-*O*-isopropylidene-D-gulose-*O*-(*tert*-butyldimethylsilyl) Oxime (16): Oxime **15** (3.9 g, 14 mmol) was dissolved in dichloromethane (70 mL), and imidazole (2.1 g, 31 mmol) and TBSCl (50 wt.-% in toluene; *d* = 0.87 g/mL at 25 °C; 5.37 mL, 15.5 mmol) were added. The resulting mixture was stirred at room temperature for 3 h. The reaction progress was monitored by TLC (hexanes/EtOAc, 1:1). After this time, water (50 mL) was added, and the mixture was vigorously stirred for a further 10 min. The organic layer was separated, and dried with $MgSO_4$, and the solvent was evaporated under reduced pressure. The product was purified by FCC (hexanes/EtOAc, 4:1) to give an inseparable (*E*)/(*Z*) mixture of **16** [5.4 g, 13.9 mmol, 99 %, (*E*)/(*Z*) ≈ 60:40] as a colourless oil. R_f(*Z*) = 0.27 and R_f(*E*) = 0.33 (both in cyclohexane/EtOAc, 4:1). ^1H NMR (600 MHz, $CDCl_3$): δ = 7.60 (d, *J* = 8.2 Hz, 0.4 H, 1-H), 7.22 (d, *J* = 4.0 Hz, 0.6 H, 1-H), 5.29 (dd, *J* = 7.4, 4.0 Hz, 0.6 H, 2-H), 4.77 (dd, *J* = 8.2, 6.9 Hz, 0.4 H, 2-H), 4.30 (dd, *J* = 7.4, 1.3 Hz, 0.6 H, 3-H), 4.27 (dd, *J* = 6.7, 4.5 Hz, 0.4 H, 3-H), 4.20 (dt, *J* = 6.7, 4.4 Hz, 0.4 H, 5-H), 4.15 (dd, *J* = 13.2, 6.6 Hz, 0.6 H, 5-H), 4.04–4.00 (m, 1 H, 6^a-H$_E$, 6^a-H$_Z$), 3.87 (dd, *J* = 8.2, 6.8 Hz, 0.4 H, 6^b-H), 3.71 (dd, *J* = 8.2, 6.8 Hz, 0.6 H, 6^b-H), 3.58 (dt, *J* = 8.5, 4.4 Hz, 0.4 H, 4-H), 3.37 (dt, *J* = 6.7, 1.9 Hz, 0.6 H, 4-H), 2.40 (d, *J* = 7.4 Hz, 0.4 H, OH), 2.28 (d, *J* = 7.3 Hz, 0.6 H, OH), 1.55 (s, 1.8 H, Me), 1.54 (s, 1.2 H, Me), 1.45 (s, 1.2 H, Me), 1.42 (s, 1.8 H, Me), 1.41 (s, 1.2 H, Me), 1.38 (s, 1.8 H, Me), 1.37 (s, 3 H, Me$_E$, Me$_Z$), 0.94 (s, 5.4 H, *t*BuSi), 0.93 (s, 3.6 H, *t*BuSi), 0.18 (s, 1.8 H, SiMe), 0.17 (s, 1.8 H, SiMe), 0.16 (s, 2.4 H, 2 SiMe) ppm. ^{13}C NMR [data for the major (*E*) isomer, extracted from the spectrum of the mixture; 150 MHz, $CDCl_3$]: δ = 154.8 (C-1), 109.7, 109.6 (2 C*Me*$_2$), 77.6 (C-3), 77.2 (C-5), 72.8 (C-2), 70.8 (C-4), 66.0 (C-6), 26.6 (Me), 26.4 (Me), 26.0 (SiC*Me*$_3$), 25.5 (Me), 24.5 (Me), 17.9 (SiCMe$_3$), –5.2 (SiMe), –5.3 (SiMe) ppm. ^{13}C NMR [data for the minor (*Z*) isomer, extracted from the spectrum of the mixture; 150 MHz, $CDCl_3$]: δ = 152.6 (C-1), 110.1, 109.7 (2 C*Me*$_2$), 78.1 (C-3), 75.9 (C-5), 75.1 (C-2), 69.3 (C-4), 65.8 (C-6), 27.2 (Me), 26.4 (Me), 26.0 (SiC*Me*$_3$), 25.2 (Me), 25.1 (Me), 18.2 (SiCMe$_3$), –5.3 (2 SiMe) ppm. MS (ESI + APCI): *m*/*z* = 390.2 ($C_{18}H_{36}NO_6Si$) $[M + H]^+$.

(*E*,*Z*)-2,3:5,6-Di-*O*-isopropylidene-4-*O*-methanesulfonyl-D-gulose-*O*-(*tert*-butyldimethylsilyl) Oxime (9): A stirred solution of oxime **16** (5.4 g, 13.9 mmol) in dichloromethane (70 mL) was cooled in ice, and then triethylamine (5.9 mL, 42 mmol) was added, followed by DMAP (515 mg, 4.2 mmol). Then, methanesulfonyl chloride (1.6 mL, 21 mmol) was added dropwise over a period of 5 min. The resulting mixture was warmed to room temperature, and stirring was continued for 12 h. When TLC showed that the reaction was complete (dichloromethane/methanol, 95:5), saturated aque-

ous NH_4Cl (50 mL) was added, and the mixture was stirred for a further 10 min. The organic layer was separated, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by FCC (hexanes/EtOAc, 7:3) to give an inseparable (*E*)/(*Z*) mixture of **9** [5.46 g, 11.7 mmol, 84 %, (*E*)/(*Z*) ≈ 55:45] as a colourless oil. R_f(*E*,*Z*) = 0.41 (cyclohexane/EtOAc, 4:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.48 (d, *J* = 8 Hz, 0.45 H, 1-H), 7.26 (d, *J* = 4.5 Hz, 0.55 H, 1-H), 5.33–5.29 (m, 0.55 H, 2-H), 4.79 (dd, *J* = 8.0, 5.8 Hz, 0.45 H, 2-H), 4.70 (dd, *J* = 8.8, 2.1 Hz, 0.45 H, 4-H), 4.62 (dd, *J* = 8.8, 5.7 Hz, 0.45 H, 3-H), 4.51–4.48 (m, 1.1 H, 3-H, 4-H), 4.34 (dd, *J* = 12.2, 6.0 Hz, 0.55 H, 5-H), 4.24 (td, *J* = 6.7, 2.0 Hz, 0.45 H, 5-H), 4.10 (dd, *J* = 8.7, 6.6 Hz, 0.55 H, 6^a-H), 4.05–3.99 (m, 0.9 H, 6^a-H, 6^b-H), 3.87 (dd, *J* = 8.7, 6.3 Hz, 0.55 H, 6^b-H), 3.16 (s, 1.65 H, OMs), 3.15 (s, 1.35 H, OMs), 1.55 (s, 1.65 H, Me), 1.52 (s, 1.35 H, Me), 1.45 (s, 1.35 H, Me), 1.44 (s, 1.65 H, Me), 1.42 (s, 1.35 H, Me), 1.38 (s, 1.65 H, Me), 1.35 (s, 1.65 H, Me), 1.34 (s, 1.35 H, Me), 0.95 (s, 4.95 H, *t*BuSi), 0.93 (s, 4.05 H, *t*BuSi), 0.20 (s, 1.65 H, SiMe), 0.19 (s, 1.65 H, SiMe), 0.16 (s, 2.7 H, 2 × SiMe) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 152.4, 151.1 (2 C-1), 110.2 (3 ×), 110.0 (4 CMe_2), 80.9, 77.0 (2 C-3), 78.9, 76.7 (2 C-4), 75.2, 73.4 (2 C-5), 74.6, 71.8 (2 C-2), 65.5, 65.4 (2 C-6), 39.5, 39.0 (2 *Me*SO_2), 28.0, 26.7, 26.1 (3 Me), 26.0 (2 Si*Me*$_3$), 25.9, 25.8, 25.7, 25.5, 25.2 (5 Me), 18.1, 18.0 (2 Si*C*Me$_3$), –5.4, –5.3 (2 ×), –5.2 (4 SiMe) ppm. MS (ESI + APCI): *m*/*z* = 468.2 ($C_{19}H_{38}NO_8SSi$) [M + H]$^+$.

(3a*R*,4*R*,6a*S*)-4-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-2,2-dimethyl-4,6a-dihydro-3a*H*-[1,3]dioxolo[4,5-*c*]pyrrole *N*-Oxide (4): Oxime **9** (5.4 g, 11.5 mmol) was placed into a reaction flask, then the flask was sealed with a rubber septum, evacuated, and filled with argon. Anhydrous THF (130 mL) was added, and the resulting solution was cooled in ice. TBAF (1 M solution in THF; 14 mL, 14 mmol) was added, and the mixture was stirred at 0 °C for 30 min. After this time, TLC showed that the reaction was complete (hexanes/EtOAc, 4:6), and the solvent was evaporated under reduced pressure. The residue was treated with brine (50 mL), and the product was extracted with ethyl acetate (4 × 50 mL). The combined organic layers were dried with $MgSO_4$ and concentrated to dryness to give the desilylated oxime together with a small amount of nitrone **4**. The mixture was then dissolved in methanol/water (4:1, v/v; 115 mL), and solid $NaHCO_3$ (7.3 g, 87 mmol) was added, followed by hydroxylamine hydrochloride (6.4 g, 92 mmol). The resulting mixture was heated at reflux for 12 h, after which time TLC showed that the reaction was complete (EtOAc). The methanol was then partially evaporated under reduced pressure. Brine (100 mL) was added, and the product was extracted with ethyl acetate (4 × 50 mL). The combined organic layers were dried with $MgSO_4$, and concentrated to dryness. The product was purified by FCC (hexanes/EtOAc, 1:4) to give nitrone **4** (2.4 g, 9.3 mmol, 81 %) as a colourless solid. R_f = 0.22 (cyclohexane/EtOAc, 1:4). M.p. 64–65 °C. $[\alpha]_D^{23}$ = –47.7 (*c* = 1.03, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 3253, 3055, 2989, 1580, 1380, 1207, 1153, 1086, 1044, 835 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.91 (pseudo t, *J* = 1.1 Hz, 1 H, 2-H), 5.23 (dt, *J* = 6.3, 1.5 Hz, 1 H, 3-H), 4.82 (d, *J* = 6.2 Hz, 1 H, 4-H), 4.77 (ddd, *J* = 7.5, 5.8, 2.7 Hz, 1 H, 6-H), 4.26 (dd, *J* = 8.9, 7.6 Hz, 1 H, 7^b-H), 4.02–4.01 (m, 1 H, 5-H), 3.96 (dd, *J* = 9.0, 5.7 Hz, 1 H, 7^a-H), 1.45 (s, 6 H, 2 Me), 1.39 (s, 3 H, Me), 1.34 (s, 3 H, Me) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 133.0 (C-2), 111.9, 110.3 (2 CMe_2), 80.8 (C-5), 79.0 (C-3), 75.1 (C-4), 71.8 (C-6), 66.0 (CH_2), 27.3 (Me), 26.1 (Me), 25.9 (Me), 24.1 (Me) ppm. HRMS (ESI): calcd. for $C_{12}H_{20}NO_5$ [M + H]$^+$ 258.1341; found 258.1332.

(4*R*,5*S*,6*S*)-6-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-4,5-isopropylidenedioxyhexahydropyrrolo[1,2-*b*]isoxazol-2-yl Acetate (3): Nitrone **1** (500 mg, 1.94 mmol) was placed into a reaction flask, followed by vinyl acetate (**2**; 10 mL). The flask was sealed, and the mixture was stirred at 75 °C for 24 h, after which time TLC showed that the reaction was complete (hexanes/EtOAc, 3:7). The solvent was then evaporated in vacuo, and the residue was purified by FCC (hexanes/EtOAc, 6:4) to give two single isoxazolidines (2*R*,3a*R*)-**3a** (80 mg, 0.23 mmol, 12 %) and (2*S*,3a*S*)-**3b** (480 mg, 1.40 mmol, 72 %), together with a mixture of **3a** and **3b** (50 mg, 0.15 mmol, 8 %). **Data for (2*R*,3a*R*)-3a:** Colourless oil. R_f = 0.44 (cyclohexane/EtOAc, 3:7). $[\alpha]_D^{25}$ = –146.87 (*c* = 1.07, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 2985, 2934, 1733, 1370, 1209, 1057, 987, 970, 866, 846 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.29 (d, *J* = 6.0 Hz, 1 H, 2-H), 4.70 (pseudo t, *J* = 7.0 Hz, 1 H, 5-H), 4.53–4.49 (m, 2 H, 4-H, 4′-H), 4.10 (dd, *J* = 8.5, 6.4 Hz, 1 H, 5′^{a}-H), 3.89 (dd, *J* = 8.5, 7.0 Hz, 1 H, 5′^{b}-H), 3.88 (dd, *J* = 7.2, 4.0 Hz, 1 H, 3a-H), 3.37–3.34 (m, 1 H, 6-H), 2.81 (ddd, *J* = 14.1, 6.6, 1.1 Hz, 1 H, 3^b-H), 2.72 (ddd, *J* = 14.1, 7.9, 2.8 Hz, 1 H, 3^a-H), 2.08 (s, 3 H, COMe), 1.52 (s, 3 H, Me), 1.46 (s, 3 H, Me), 1.39 (s, 3 H, Me), 1.31 (s, 3 H, Me) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.7 (C=O), 115.2 (CMe_2), 109.6 (CMe_2), 94.6 (C-2), 88.1 (C-4), 82.7 (C-5), 75.7 (C-6), 73.9 (C-4′), 70.5 (C-3a), 66.4 (C-5′), 41.4 (C-3), 27.4 (Me), 26.8 (Me), 25.5 (Me), 25.0 (Me), 21.3 (CO*Me*) ppm. HRMS (ESI): calcd. for $C_{16}H_{26}NO_7$ [M + H]$^+$ 344.1709; found 344.1701. **Data for (2*S*,3a*S*)-3b:** Colourless solid. R_f = 0.52 (cyclohexane/EtOAc, 3:7). M.p. 84–85 °C. $[\alpha]_D^{25}$ = +144.45 (*c* = 1.04, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 2989, 2936, 1732, 1371, 1237, 1202, 1072, 1051, 976, 853 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.25 (dd, *J* = 6.4, 2.2 Hz, 1 H, 2-H), 4.84 (d, *J* = 6.3 Hz, 1 H, 5-H), 4.66 (pseudo t, *J* = 5.8 Hz, 1 H, 4-H), 4.24 (td, *J* = 7.3, 3.5 Hz, 1 H, 4′-H), 4.05–4.01 (m, 2 H, 5′^{a}-H, 5′^{b}-H), 3.91–3.88 (m, 1 H, 3a-H), 3.81 (d, *J* = 2.8 Hz, 1 H, 6-H), 3.00 (ddd, *J* = 13.5, 6.5, 1.8 Hz, 1 H, 3^b-H), 2.46 (ddd, *J* = 13.4, 8.1, 2.3 Hz, 1 H, 3^a-H), 2.07 (s, 3 H, COMe), 1.48 (s, 3 H, Me), 1.39 (s, 3 H, Me), 1.33 (s, 3 H, Me), 1.30 (s, 3 H, Me) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.7 (C=O), 113.0 (CMe_2), 109.3 (CMe_2), 96.1 (C-2), 86.0 (C-5), 82.4 (C-4), 76.1 (C-4′), 71.5 (C-6), 69.0 (C-3a), 66.3 (C-5′), 37.7 (C-3), 26.5 (Me), 26.1 (Me), 25.3 (Me), 24.2 (Me), 21.4 (CO*Me*) ppm. HRMS (ESI): calcd. for $C_{16}H_{26}NO_7$ [M + H]$^+$ 344.1709; found 344.1701.

(4*R*,5*S*,6*S*)-6-{[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-4,5-isopropylidenedioxyhexahydropyrrolo[1,2-*b*]isoxazol-2-yl}methyl Benzoate (18): Nitrone **1** (500 mg, 1.94 mmol) was placed into a reaction flask, followed by toluene (10 mL) and allyl benzoate (**5**; 630 mg, 3.9 mmol), which was prepared according to ref.[15] The flask was sealed, and the mixture was stirred at 80 °C for 48 h. After TLC showed that the reaction was complete (hexanes/EtOAc, 3:7), the mixture was concentrated to dryness, and the products were isolated by FCC (hexanes/EtOAc, 7:3) to give two single isomers (2*S*,3a*S*)-**18b** (490 mg, 1.17 mmol, 60 %) and (2*R*,3a*S*)-**18d** (35 mg, 0.08 mmol, 4 %), together with a mixture of three isoxazolidines (2*R*,3a*R*)-**18a**, **18b**, and **18d** (90 mg, 0.22 mmol, 11 %). With the aim of complete characterization of new compounds, a sample of the mixture was subjected to repeated preparative TLC (hexanes/acetone, 9:1) to give pure isomer **18a**. **Data for (2*R*,3a*R*)-18a:** Pale yellow syrup. R_f = 0.56 (cyclohexane/EtOAc, 3:7). $[\alpha]_D^{25}$ = –74.73 (*c* = 1.15, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 2983, 2934, 1717, 1452, 1371, 1267, 1207, 1064, 1026, 868, 711 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.07–8.03 (m, 2 H, Ph-H), 7.58–7.43 (m, 3 H, Ph-H), 4.70 (pseudo t, *J* = 7.0 Hz, 1 H, 5-H), 4.57–4.51 (m, 2 H, 4-H, 4′-H), 4.43–4.35 (m, 2 H, 2-H, CH_2OBz), 4.31 (dd, *J* = 10.2, 3.6 Hz, 1 H, CH_2OBz), 4.09 (dd, *J* = 8.4, 6.3 Hz, 1 H, 5′^{a}-H), 3.89 (dd, *J* = 8.3, 7.6 Hz, 1 H, 5′^{b}-H), 3.85 (dd, *J* = 6.8, 3.2 Hz, 1 H, 3a-H), 3.35 (pseudo t, *J* = 7.9 Hz, 1 H, 6-H), 2.55 (dd, *J* = 12.7, 7.1 Hz, 1 H, 3^b-H), 2.43–2.36 (m, 1 H, 3^a-H), 1.52 (s, 3 H, Me), 1.47 (s, 3 H, Me), 1.39 (s, 3 H, Me), 1.31 (s, 3 H, Me) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.3 (C=O), 133.1 (CH-Ph), 130.0 (C-Ph), 129.7 (CH-Ph), 128.4 (CH-Ph), 115.0 (CMe_2), 109.4 (CMe_2), 87.8 (C-4), 83.0 (C-5), 75.4 (C-6), 74.6 (C-2), 74.2 (C-4′), 71.0 (C-3a), 66.5 (C-5′), 66.1 (CH_2OBz), 36.7 (C-3), 27.5 (Me), 26.8 (Me), 25.6 (Me), 25.1 (Me) ppm. HRMS (ESI): calcd. for $C_{22}H_{30}NO_7$ [M + H]$^+$ 420.2022; found 420.2013. **Data for (2*S*,3a*S*)-18b:** Colourless solid. R_f = 0.56

(cyclohexane/EtOAc, 3:7). M.p. 109–110 °C. $[\alpha]_D^{25}$ = +62.74 (*c* = 1.00, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 2987, 2937, 1713, 1452, 1379, 1270, 1205, 1054, 1026, 871, 715 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.08–8.04 (m, 2 H, Ph-H), 7.58–7.40 (m, 3 H, Ph-H), 4.75 (dd, *J* = 6.4, 2.6 Hz, 1 H, 5-H), 4.69 (pseudo t, *J* = 6.4, 5.6 Hz, 1 H, 4-H), 4.52 (ddd, *J* = 11.2, 7.9, 5.8 Hz, 1 H, 2-H), 4.41–4.32 (m, 2 H, CH_2OBz), 4.28 (ddd, *J* = 7.3, 6.5, 3.7 Hz, 1 H, 4′-H), 4.07–3.98 (m, 2 H, 5′^{a}-H, 5′^{b}-H), 3.87 (ddd, *J* = 8.6, 5.5, 3.1 Hz, 1 H, 3a-H), 3.59 (pseudo t, *J* = 3.2, 3.0 Hz, 1 H, 6-H), 2.73 (ddd, *J* = 12.4, 8.0, 3.1 Hz, 1 H, 3^b-H), 2.16 (ddd, *J* = 12.5, 8.6, 6.2 Hz, 1 H, 3^a-H), 1.52 (s, 3 H, Me), 1.40 (s, 3 H, Me), 1.34 (s, 3 H, Me), 1.33 (s, 3 H, Me) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.5 (C=O), 133.0 (CH-Ph), 130.0 (C-Ph), 129.7 (CH-Ph), 128.3 (CH-Ph), 113.0 (CMe_2), 109.4 (CMe_2), 84.3 (C-5), 81.3 (C-4), 76.3 (C-4′), 75.0 (C-2), 71.0 (C-6), 68.3 (C-3a), 66.2 (C-5′), 65.9 (CH_2OBz), 32.9 (C-3), 26.5 (Me), 26.2 (Me), 25.3 (Me), 24.4 (Me) ppm. HRMS (ESI): calcd. for $C_{22}H_{30}NO_7$ $[M + H]^+$ 420.2022; found 420.2012. **Data for (2*R*,3a*S*)-18d:** Colourless syrup. R_f = 0.51 (cyclohexane/EtOAc, 3:7). $[\alpha]_D^{25}$ = +21.32 (*c* = 1.04, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 2983, 2935, 1718, 1452, 1370, 1268, 1206, 1070, 1027, 869, 711 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.08–8.06 (m, 2 H, Ph-H), 7.57–7.42 (m, 3 H, Ph-H), 4.78 (dd, *J* = 6.4, 2.1 Hz, 1 H, 5-H), 4.70 (pseudo t, *J* = 6.2, 5.7 Hz, 1 H, 4-H), 4.54 (dd, *J* = 11.5, 3.8 Hz, 1 H, CH_2OBz), 4.47 (dd, *J* = 11.5, 7.4 Hz, 1 H, CH_2OBz), 4.40 (ddd, *J* = 15.4, 7.7, 3.7 Hz, 1 H, 2-H), 4.22 (ddd, *J* = 7.4, 6.6, 4.2 Hz, 1 H, 4′-H), 4.04 (dd, *J* = 8.0, 6.5 Hz, 1 H, 5′^{a}-H), 4.00 (pseudo t, *J* = 7.9, 7.8 Hz, 1 H, 5′^{b}-H), 3.86–3.82 (m, 1 H, 3a-H), 3.72 (dd, *J* = 4.1, 2.0 Hz, 1 H, 6-H), 2.47–2.42 (m, 1 H, 3^b-H), 2.39 (ddd, *J* = 12.3, 8.3, 4.2 Hz, 1 H, 3^a-H), 1.54 (s, 3 H, Me), 1.40 (s, 3 H, Me), 1.34 (s, 3 H, Me), 1.32 (s, 3 H, Me) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.4 (C=O), 133.0 (CH-Ph), 130.0 (C-Ph), 129.8 (CH-Ph), 128.3 (CH-Ph), 113.2 (CMe_2), 109.4 (CMe_2), 85.6 (C-5), 82.1 (C-4), 76.3 (C-4′), 76.1 (C-2), 71.6 (C-6), 68.5 (C-3a), 66.4 (C-5′), 65.2 (CH_2OBz), 32.5 (C-3), 26.4 (Me), 26.2 (Me), 25.3 (Me), 24.2 (Me) ppm. HRMS (ESI): calcd. for $C_{22}H_{30}NO_7$ $[M + H]^+$ 420.2022; found 420.2013.

Methyl (4*R*,5*S*,6*S*)-6-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-4,5-isopropylidenedioxyhexahydropyrrolo[1,2-*b*]isoxazole-2-carboxylate (19): Nitrone **1** (200 mg, 0.78 mmol) was placed into a reaction flask, followed by toluene (8 mL) and methyl acrylate (**6**; 0.35 mL, 3.9 mmol). The flask was sealed, and the mixture was stirred at 80 °C for 24 h, after which time TLC showed that the reaction was complete (hexanes/EtOAc, 3:7). The mixture was then concentrated in vacuo, and the residue was purified by FCC (hexanes/EtOAc, 6:4) to give one pure isoxazolidine (2*R*,3a*R*)-**19a** (45 mg, 0.13 mmol, 16 %), and an inseparable mixture of two isoxazolidines (2*S*,3a*S*)-**19b** and (2*R*,3a*S*)-**19d** (200 mg, 0.58 mmol, 74 %). **Data for (2*R*,3a*R*)-19a:** Pale yellow oil. R_f = 0.37 (cyclohexane/EtOAc, 3:7). $[\alpha]_D^{25}$ = –64.09 (*c* = 1.01, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 2985, 2937, 1749, 1749, 1734, 1371, 1206, 1156, 1059, 1024, 851 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.73 (pseudo t, *J* = 7.0 Hz, 1 H, 5-H), 4.60–4.52 (m, 3 H, 4-H, 2-H, 4′-H), 4.13 (dd, *J* = 8.5, 6.3 Hz, 1 H, 5′^{a}-H), 3.91 (dd, *J* = 8.5, 7.2 Hz, 1 H, 5′^{b}-H), 3.81 (dd, *J* = 7.6, 3.6 Hz, 1 H, 3a-H), 3.76 (s, 3 H, CO_2Me), 3.37 (pseudo t, *J* = 7.6 Hz, 1 H, 6-H), 2.90 (ddd, *J* = 13.1, 7.6, 5.5 Hz, 1 H, 3^a-H), 2.72 (ddd, *J* = 13.2, 9.1, 1.2 Hz, 1 H, 3^b-H), 1.51 (s, 3 H, Me), 1.47 (s, 3 H, Me), 1.41 (s, 3 H, Me), 1.31 (s, 3 H, Me) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 172.2 (C=O), 115.2 (CMe_2), 109.5 (CMe_2), 87.9 (C-4), 82.9 (C-5), 75.4 (C-6), 74.3 (C-4′), 74.1 (C-2), 70.9 (C-3a), 66.5 (C-5′), 52.5 (CO_2Me), 37.6 (C-3), 27.4 (Me), 26.7 (Me), 25.6 (Me), 25.0 (Me) ppm. HRMS (ESI): calcd. for $C_{16}H_{26}NO_7$ $[M + H]^+$ 344.1709; found 344.1701. The NMR spectra of **19b** and **19d** are not reported here due to the low clarity of the signals in the spectra of the mixture. In order to determine the diastereoselectivity of the above-mentioned 1,3-dipolar cycloaddition and to assign the configuration of the remaining isomers **19b** and **19d**, the reaction was repeated under identical conditions, and then the crude product mixture (280 mg) was subjected to reduction with $LiAlH_4$ (35 mg, 0.9 mmol) in anhydrous THF (8 mL) with stirring under argon at 0 °C for 1 h. When TLC showed that the starting isoxazolidines had disappeared (EtOAc), the reaction was quenched by the addition of a few drops of water, followed by a saturated aqueous solution of Rochelle salt (10 mL) and diethyl ether (10 mL). The resulting mixture was stirred well for 30 min, then the organic layer was separated, and the aqueous layer was extracted with diethyl ether (10 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to give a crude mixture of the corresponding alcohols (220 mg), which were subsequently benzoylated as follows. The residue was dissolved in dichloromethane (7 mL). DMAP (8 mg, 0.07 mmol), pyridine (155 µL, 1.9 mmol), and benzoyl chloride (115 µL, 1 mmol) were added, and the solution was stirred at room temperature for 24 h. After this time, TLC showed that the reaction was complete (hexanes/EtOAc, 1:4), and saturated aqueous $NaHCO_3$ (5 mL) and water (10 mL) were added. The mixture was stirred vigorously for 10 min. The organic layer was separated, and the aqueous layer was extracted with dichloromethane (5 mL). The combined organic layers were dried with $MgSO_4$, and the solvent was evaporated under reduced pressure. The residue was purified by FCC (hexanes/EtOAc, 65:35) to give three single isomers (2*R*,3a*R*)-**18a** (45 mg, 0.10 mmol, 13 %), (2*S*,3a*S*)-**18b** (110 mg, 0.26 mmol, 33 %), and (2*R*,3a*S*)-**18d** (10 mg, 0.02 mmol, 3 %), along with a mixture of **18a** and **18b** (55 mg, 0.13 mmol, 17 %) in an overall yield of 66 % over three steps. The analytical data of all isomers **18a**, **18b**, and **18d** were consistent with those reported above. The ratio determined from the ^1H NMR spectrum of the crude mixture was **18a**/**18b**/**18d** = 20:50:30.

(4*R*,5*S*,6*S*)-6-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-4,5-isopropylidenedioxyhexahydropyrrolo[1,2-*b*]isoxazole-2-carbonitrile (20): Nitrone **1** (500 mg, 1.94 mmol) was placed into a reaction flask, followed by toluene (10 mL) and acrylonitrile (**7**; 0.64 mL, 9.7 mmol). The flask was sealed, and the mixture was stirred at 80 °C for 24 h, after which time TLC showed that the reaction was complete (hexanes/EtOAc, 3:7). The mixture was then concentrated to dryness, and the residue was purified by FCC (hexanes/EtOAc, 65:35) to give one single isoxazolidine (2*S*,3a*S*)-**20b** (250 mg, 0.80 mmol, 41 %), along with a mixture of two isoxazolidines (2*R*,3a*R*)-**20a** and (2*R*,3a*S*)-**20d** (230 mg, 0.74 mmol, 38 %). With the aim of complete characterization of new compounds, a sample was subjected to repeated preparative TLC (hexanes/acetone, 95:5) to give pure isomers **20a** and **20d**. **Data for (2*R*,3a*R*)-20a:** Colourless oil. R_f = 0.55 (cyclohexane/EtOAc, 3:7). $[\alpha]_D^{25}$ = –122.74 (*c* = 0.33, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 2985, 2937, 1372, 1254, 1208, 1155, 1059, 1034, 866, 848 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 4.82 (dd, *J* = 8.9, 3.9 Hz, 1 H, 2-H), 4.69 (pseudo t, *J* = 6.9 Hz, 1 H, 5-H), 4.53–4.45 (m, 2 H, 4′-H, 4-H), 4.10 (dd, *J* = 8.6, 6.3 Hz, 1 H, 5′^{a}-H), 3.97–3.85 (m, 2 H, 5′^{b}-H, 3a-H), 3.43 (pseudo t, *J* = 7.6 Hz, 1 H, 6-H), 2.98 (ddd, *J* = 13.2, 8.1, 3.9 Hz, 1 H, 3^a-H), 2.77 (ddd, *J* = 13.3, 9.0, 1.7 Hz, 1 H, 3^b-H), 1.52 (s, 3 H, Me), 1.48 (s, 3 H, Me), 1.40 (s, 3 H, Me), 1.30 (s, 3 H, Me) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 118.4 (CN), 115.5 (CMe_2), 109.7 (CMe_2), 87.9 (C-4), 82.6 (C-5), 75.0 (C-4′), 73.8 (C-6), 70.1 (C-3a), 66.4 (C-5′), 64.1 (C-2), 40.0 (C-3), 27.4 (Me), 26.7 (Me), 25.4 (Me), 25.0 (Me) ppm. HRMS (ESI): calcd. for $C_{15}H_{23}N_2O_5$ $[M + H]^+$ 311.1607; found 311.1600. **Data for (2*S*,3a*S*)-20b:** Colourless solid. R_f = 0.64 (cyclohexane/EtOAc, 3:7). M.p. 137–138 °C. $[\alpha]_D^{25}$ = +90.67 (*c* = 1.00, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 2987, 2889, 1370, 1253, 1208, 1157, 1086, 1057, 1035, 863 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.88 (dd, *J* = 6.2, 1.3 Hz, 1 H, 5-H), 4.75 (dd, *J* = 8.7, 4.5 Hz, 1 H, 2-H), 4.67 (pseudo t, *J* = 5.9, 5.7 Hz, 1 H, 4-H), 4.24 (ddd, *J* = 7.7, 6.9, 2.8 Hz, 1 H, 4′-H), 4.14–4.01 (m, 2 H, 5′^{a}-H, 5′^{b}-H), 3.96–3.90 (m, 1 H, 3a-H), 3.77 (d, *J* = 2.6 Hz, 1 H, 6-H), 3.04 (ddd, *J* = 12.5, 9.0, 2.0 Hz, 1 H, 3^b-H), 2.70

(ddd, *J* = 12.6, 8.5, 4.2 Hz, 1 H, 3^{a}-H), 1.43 (s, 3 H, Me), 1.38 (s, 3 H, Me), 1.34 (s, 3 H, Me), 1.30 (s, 3 H, Me) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 119.3 (CN), 113.0 (*C*Me$_2$), 109.5 (*C*Me$_2$), 86.5 (C-5), 82.4 (C-4), 76.3 (C-4′), 70.8 (C-6), 68.5 (C-3a), 66.3 (C-5′), 64.2 (C-2), 36.1 (C-3), 26.5 (Me), 26.0 (Me), 25.6 (Me), 24.1 (Me) ppm. HRMS (ESI): calcd. for $C_{15}H_{23}N_2O_5$ [M + H]$^+$ 311.1607; found 311.1601. **Data for (2*R*,3a*S*)-20d:** Colourless solid. R_f = 0.55 (cyclohexane/EtOAc, 3:7). M.p. 107–108 °C. $[\alpha]_D^{25}$ = +85.04 (*c* = 0.87, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 2983, 2937, 1371, 1251, 1207, 1158, 1052, 989, 878, 844 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.79 (dd, *J* = 6.3, 1.9 Hz, 1 H, 5-H), 4.71 (pseudo t, *J* = 5.8 Hz, 1 H, 4-H), 4.62 (dd, *J* = 9.2, 6.8 Hz, 1 H, 2-H), 4.22 (td, *J* = 7.0, 4.0 Hz, 1 H, 4′-H), 4.05 (dd, *J* = 8.0, 6.7 Hz, 1 H, 5′^{a}-H), 3.97 (dd, *J* = 7.9, 7.5 Hz, 1 H, 5′^{b}-H), 3.88 (ddd, *J* = 8.5, 5.2, 3.0 Hz, 1 H, 3a-H), 3.77 (dd, *J* = 3.7, 1.8 Hz, 1 H, 6-H), 2.96 (ddd, *J* = 12.5, 6.8, 3.0 Hz, 1 H, 3^{a}-H), 2.76 (dt, *J* = 12.5, 9.0 Hz, 1 H, 3^{b}-H), 1.61 (s, 3 H, Me), 1.39 (s, 3 H, Me), 1.33 (s, 6 H, 2 Me) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 117.4 (CN), 113.7 (*C*Me$_2$), 109.6 (*C*Me$_2$), 85.3 (C-5), 81.5 (C-4), 75.9 (C-4′), 71.4 (C-6), 68.8 (C-3a), 66.3 (C-5′), 63.8 (C-2), 35.2 (C-3), 26.4 (Me), 26.1 (Me), 25.1 (Me), 24.2 (Me) ppm. HRMS (ESI): calcd. for $C_{15}H_{23}N_2O_5$ [M + H]$^+$ 311.1607; found 311.1600.

(4*S*,5*R*,6*R*)-6-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-4,5-isopropylidenedioxyhexahydropyrrolo[1,2-*b*]isoxazol-2-yl Acetate (17): Nitrone **4** (500 mg, 1.94 mmol) was placed into a reaction flask, followed by vinyl acetate (**2**; 10 mL). The flask was sealed, and the mixture was stirred at 75 °C for 24 h, after which time TLC showed that the reaction was complete (hexanes/EtOAc, 3:7). The solvent was then evaporated in vacuo, and the residue was purified by FCC (hexanes/EtOAc, 6:4) to give two single isoxazolidines (2*S*,3a*S*)-**17a** (320 mg, 0.93 mmol, 48 %) and (2*R*,3a*R*)-**17b** (90 mg, 0.26 mmol, 13 %), along with a mixture of **17a** and **17b** (180 mg, 0.52 mmol, 27 %). **Data for (2*S*,3a*S*)-17a:** Colourless syrup. R_f = 0.53 (cyclohexane/EtOAc, 3:7). $[\alpha]_D^{25}$ = +159.96 (*c* = 1.00, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 2985, 2937, 1741, 1371, 1227, 1208, 1064, 1009, 972, 842 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.32–6.26 (m, 1 H, 2-H), 4.96 (pseudo t, *J* = 6.5 Hz, 1 H, 5-H), 4.56 (dd, *J* = 6.8, 3.7 Hz, 1 H, 4-H), 4.46 (dt, *J* = 8.5, 5.7 Hz, 1 H, 4′-H), 4.13 (dd, *J* = 8.5, 5.9 Hz, 1 H, 5′^{a}-H), 4.01 (dd, *J* = 8.5, 5.6 Hz, 1 H, 5′^{b}-H), 3.88–3.79 (m, 1 H, 3a-H), 3.38–3.30 (m, 1 H, 6-H), 2.79 (ddd, *J* = 14.1, 6.4, 1.7 Hz, 1 H, 3^{b}-H), 2.65 (ddd, *J* = 14.1, 7.7, 2.5 Hz, 1 H, 3^{a}-H), 2.07 (s, 3 H, COMe), 1.53 (s, 3 H, Me), 1.47 (s, 3 H, Me), 1.38 (s, 3 H, Me), 1.33 (s, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.4 (C=O), 115.0 (*C*Me$_2$), 109.8 (*C*Me$_2$), 94.8 (C-2), 88.3 (C-5), 85.0 (C-4), 75.1 (C-4′), 75.0 (C-6), 70.5 (C-3a), 67.9 (C-5′), 41.2 (C-3), 27.2 (Me), 26.9 (Me), 25.6 (Me), 24.8 (Me), 21.2 (CO*Me*) ppm. HRMS (ESI): calcd. for $C_{16}H_{26}NO_7$ [M + H]$^+$ 344.1709; found 344.1701. **Data for (2*R*,3a*R*)-17b:** Colourless syrup. R_f = 0.47 (cyclohexane/EtOAc, 3:7). $[\alpha]_D^{25}$ = –104.43 (*c* = 1.05, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 2985, 2937, 1740, 1372, 1233, 1206, 1070, 1056, 979, 857 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.27 (dd, *J* = 6.5, 2.3 Hz, 1 H, 2-H), 4.85 (dd, *J* = 6.4, 1.0 Hz, 1 H, 5-H), 4.62 (pseudo t, *J* = 6.0, 5.7 Hz, 1 H, 4-H), 4.28 (td, *J* = 6.7, 3.8 Hz, 1 H, 4′-H), 4.14 (dd, *J* = 8.6, 7.2 Hz, 1 H, 5′^{a}-H), 3.97–3.90 (m, 1 H, 3a-H), 3.86 (dd, *J* = 8.5, 6.3 Hz, 1 H, 5′^{b}-H), 3.77 (d, *J* = 3.4 Hz, 1 H, 6-H), 3.03 (ddd, *J* = 13.6, 6.5, 1.9 Hz, 1 H, 3^{b}-H), 2.48 (ddd, *J* = 13.6, 8.0, 2.4 Hz, 1 H, 3^{a}-H), 2.08 (s, 3 H, COMe), 1.48 (s, 3 H, Me), 1.42 (s, 3 H, Me), 1.31 (s, 3 H, Me), 1.30 (s, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.6 (C=O), 112.9 (*C*Me$_2$), 109.8 (*C*Me$_2$), 96.3 (C-2), 83.4 (C-5), 82.5 (C-4), 75.1 (C-4′), 73.1 (C-6), 68.4 (C-3a), 67.1 (C-5′), 37.5 (C-3), 26.5 (Me), 26.4 (Me), 24.5 (Me), 24.1 (Me), 21.4 (CO*Me*) ppm. HRMS (ESI): calcd. for $C_{16}H_{26}NO_7$ [M + H]$^+$ 344.1709; found 344.1705.

(4*S*,5*R*,6*R*)-6-{[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-4,5-isopropylidenedioxyhexahydropyrrolo[1,2-*b*]isoxazol-2-yl}methyl Benzoate (21): Nitrone **4** (350 mg, 1.36 mmol) was placed into a reaction flask, followed by toluene (7 mL) and allyl benzoate (**5**; 440 mg, 2.7 mmol), which was prepared according to ref.[15] The flask was sealed, and the mixture was stirred at 80 °C for 48 h. After this time, TLC showed that the reaction was complete (hexanes/EtOAc, 3:7). The mixture was concentrated to dryness, and the residue was purified by FCC (hexanes/EtOAc, 7:3) to give two single isoxazolidines (2*S*,3a*S*)-**21a** (280 mg, 0.67 mmol, 49 %) and (2*R*,3a*R*)-**21b** (95 mg, 0.23 mmol, 17 %), along with a mixture of **21a** and **21b** (90 mg, 0.21 mmol, 15 %). **Data for (2*S*,3a*S*)-21a:** Colourless solid. R_f = 0.58 (cyclohexane/EtOAc, 3:7). M.p. 97–98 °C. $[\alpha]_D^{25}$ = +118.37 (*c* = 1.00, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 2981, 2934, 1710, 1452, 1370, 1259, 1210, 1068, 1024, 847, 714 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.04 (d, *J* = 7.8 Hz, 2 H, Ph-H), 7.57 (t, *J* = 7.5 Hz, 1 H, Ph-H), 7.45 (t, *J* = 7.8 Hz, 1 H, Ph-H), 4.96 (pseudo t, *J* = 6.5 Hz, 1 H, 5-H), 4.60 (dd, *J* = 6.7, 3.9 Hz, 1 H, 4-H), 4.46–4.39 (m, 2 H, 4′-H, 2-H), 4.35 (dd, *J* = 11.2, 7.7 Hz, 1 H, C*H*$_2$OBz), 4.19 (dd, *J* = 11.3, 3.9 Hz, 1 H, C*H*$_2$OBz), 4.12 (dd, *J* = 8.6, 6.0 Hz, 1 H, 5′^{a}-H), 4.01 (dd, *J* = 8.6, 5.7 Hz, 1 H, 5′^{b}-H), 3.74 (dd, *J* = 7.2, 3.7 Hz, 1 H, 3a-H), 3.30 (dd, *J* = 8.4, 6.5 Hz, 1 H, 6-H), 2.54 (dd, *J* = 12.9, 8.2 Hz, 1 H, 3^{b}-H), 2.33 (ddd, *J* = 12.9, 7.5, 5.3 Hz, 1 H, 3^{a}-H), 1.53 (s, 3 H, Me), 1.47 (s, 3 H, Me), 1.37 (s, 3 H, Me), 1.34 (s, 3 H, Me) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.4 (C=O), 133.2 (CH-Ph), 130.1 (C-Ph), 129.8 (CH-Ph), 128.5 (CH-Ph), 115.1 (*C*Me$_2$), 109.8 (*C*Me$_2$), 88.6 (C-4), 85.6 (C-5), 75.6 (C-4′), 75.0 (C-2), 74.8 (C-6), 71.1 (C-3a), 68.1 (C-5′), 65.7 (*C*H$_2$OBz), 36.3 (C-3), 27.4 (Me), 27.0 (Me), 25.7 (Me), 24.9 (Me) ppm. HRMS (ESI): calcd. for $C_{22}H_{30}NO_7$ [M + H]$^+$ 420.2022; found 420.2014. **Data for (2*R*,3a*R*)-21b:** Colourless syrup. R_f = 0.52 (cyclohexane/EtOAc, 3:7). $[\alpha]_D^{25}$ = –40.62 (*c* = 1.05, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 2985, 2935, 1717, 1452, 1371, 1269, 1206, 1068, 1026, 850, 711 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.07–8.04 (m, 2 H, Ph-H), 7.58–7.41 (m, 3 H, Ph-H), 4.78 (dd, *J* = 6.4, 2.8 Hz, 1 H, 5-H), 4.67 (pseudo t, *J* = 6.2, 5.9 Hz, 1 H, 4-H), 4.55–4.51 (m, 1 H, 2-H), 4.37–4.34 (m, 2 H, C*H*$_2$OBz), 4.20 (dd, *J* = 11.8, 6.4 Hz, 1 H, 4′-H), 4.12 (dd, *J* = 8.5, 6.8 Hz, 1 H, 5′^{a}-H), 3.91 (dd, *J* = 8.5, 6.3 Hz, 1 H, 5′^{b}-H), 3.86 (ddd, *J* = 8.6, 5.6, 3.3 Hz, 1 H, 3a-H), 3.48 (dd, *J* = 5.0, 2.8 Hz, 1 H, 6-H), 2.74 (ddd, *J* = 12.4, 8.1, 3.3 Hz, 1 H, 3^{b}-H), 2.16 (ddd, *J* = 12.6, 8.6, 6.1 Hz, 1 H, 3^{a}-H), 1.52 (s, 3 H, Me), 1.44 (s, 3 H, Me), 1.34 (s, 3 H, Me), 1.33 (s, 3 H, Me) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.4 (C=O), 133.0 (CH-Ph), 130.0 (C-Ph), 129.7 (CH-Ph), 128.3 (CH-Ph), 113.0 (*C*Me$_2$), 109.6 (*C*Me$_2$), 82.6 (C-5), 81.0 (C-4), 75.8 (H-4′), 75.2 (C-2), 72.4 (H-6), 67.6 (C-3a), 67.2 (C-5′), 65.8 (*C*H$_2$OBz), 32.7 (C-3), 26.6 (Me), 26.5 (Me), 24.9 (Me), 24.4 (Me) ppm. HRMS (ESI): calcd. for $C_{22}H_{30}NO_7$ [M + H]$^+$ 420.2022; found 420.2015.

Methyl (4*S*,5*R*,6*R*)-6-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-4,5-isopropylidenedioxyhexahydropyrrolo[1,2-*b*]isoxazole-2-carboxylate (22): Nitrone **4** (200 mg, 0.78 mmol) was placed into a reaction flask, followed by toluene (8 mL) and methyl acrylate (**6**; 0.35 mL, 3.9 mmol). The flask was sealed, and the mixture was stirred at 80 °C for 24 h, after which time TLC showed that the reaction was complete (hexanes/EtOAc, 3:7). The mixture was then concentrated in vacuo, and the residue was purified by FCC (hexanes/EtOAc, 6:4) to give one single isoxazolidine (2*S*,3a*S*)-**22a** (175 mg, 0.51 mmol, 65 %), along with an inseparable mixture of (2*R*,3a*R*)-**22b** and an unidentified isomer (85 mg, 0.24 mmol, 31 %). **Data for (2*S*,3a*S*)-22a:** Colourless solid. R_f = 0.52 (cyclohexane/EtOAc, 3:7). M.p. 74–75 °C. $[\alpha]_D^{25}$ = +104.45 (*c* = 0.98, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 2989, 2936, 1749, 1733, 1373, 1202, 1157, 1060, 1027, 855 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.97 (pseudo t, *J* = 6.4 Hz, 1 H, 5-H), 4.60 (dd, *J* = 6.5, 4.1 Hz, 1 H, 4-H), 4.52 (dd, *J* = 9.2, 4.2 Hz, 1 H, 2-H), 4.51–4.46 (m, 1 H, 4′-H), 4.24 (dd, *J* = 8.6, 5.9 Hz, 1 H, 5′^{a}-H), 4.04 (dd, *J* = 8.2, 6.3 Hz, 1 H, 5′^{b}-H), 3.75–3.72 (m, 4 H, CO_2*Me*, 3a-H), 3.31 (dd, *J* = 8.6, 6.2 Hz, 1 H, 6-H), 2.86 (ddd, *J* = 12.4, 7.8, 4.3 Hz, 1 H, 3^{a}-H), 2.70–2.65 (m, 1 H, 3^{b}-H), 1.52 (s, 3 H, Me), 1.47 (s, 3 H, Me), 1.40 (s, 3 H, Me), 1.34 (s, 3 H, Me) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ =

172.3 (C=O), 115.1 (*C*Me$_2$), 109.8 (*C*Me$_2$), 88.6 (C-4), 85.6 (C-5), 75.5 (C-4′), 74.9 (C-6), 74.4 (C-2), 70.7 (C-3a), 68.0 (C-5′), 52.3 (CO$_2$*Me*), 37.5 (C-3), 27.3 (Me), 26.9 (Me), 25.7 (Me), 24.8 (Me) ppm. HRMS (ESI): calcd. for $C_{16}H_{26}NO_7$ [M + H]$^+$ 344.1709; found 344.1705. The NMR spectra of **22b** and the unidentified isomer are not reported here due to the low clarity of the signals in the spectra of the mixture. In order to determine the diastereoselectivity of the above-mentioned 1,3-dipolar cycloaddition and to assign the configuration of all remaining isomers, the reaction was repeated under identical conditions, and the crude product mixture (275 mg) was then subjected to reduction with $LiAlH_4$ (35 mg, 0.9 mmol) in anhydrous THF (8 mL) with stirring under argon at 0 °C for 1 h. When TLC showed that the starting isoxazolidines had disappeared (EtOAc), the reaction was quenched by the addition of a few drops of water, followed by a saturated aqueous solution of Rochelle salt (10 mL) and diethyl ether (10 mL). The resulting mixture was stirred well for 30 min, then the organic layer was separated, and the aqueous layer was extracted with diethyl ether (10 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to give a crude mixture of the corresponding alcohols (210 mg), which were subsequently benzoylated as follows. The residue was dissolved in dichloromethane (7 mL). DMAP (8 mg, 0.07 mmol), pyridine (155 μL, 1.9 mmol), and benzoyl chloride (115 μL, 1 mmol) were added, and the solution was stirred at room temperature for 24 h. After this time, TLC showed that the reaction was complete (hexanes/EtOAc, 1:4). Saturated aqueous $NaHCO_3$ (5 mL) and water (10 mL) were added, and the mixture was stirred vigorously for 10 min. The organic layer was separated, and the aqueous layer was extracted with dichloromethane (5 mL). The combined organic layers were dried with $MgSO_4$, and the solvent was evaporated under reduced pressure. The residue was purified by FCC (hexanes/EtOAc, 65:35) to give two single isomers (2*S*,3a*S*)-**21a** (145 mg, 0.34 mmol, 44 %) and (2*R*,3a*R*)-**21b** (75 mg, 0.18 mmol, 23 %) in an overall yield of 67 % over three steps. Unfortunately, the third cycloadduct was not isolated, and therefore was not characterized. The analytical data of **21a** and **21b** were consistent with those reported above. The ratio determined from the ^{1}H NMR spectrum of the crude mixture was **21a**/**21b** = 75:25.

(4*S*,5*R*,6*R*)-6-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-4,5-isopropylidenedioxyhexahydropyrrolo[1,2-*b*]isoxazole-2-carbonitrile (23): Nitrone **4** (900 mg, 3.5 mmol) was placed into a reaction flask, followed by toluene (17 mL) and acrylonitrile (**7**; 1.15 mL, 17.5 mmol). The flask was sealed, and the mixture was stirred at 80 °C for 24 h, after which time TLC showed that the reaction was complete (hexanes/EtOAc, 3:7). The mixture was then concentrated to dryness, and the residue was purified by FCC (hexanes/EtOAc, 6:4) to give a single isoxazolidine (2*R*,3a*R*)-**23b** (40 mg, 0.13 mmol, 4 %). Also isolated were a fraction consisting of two isoxazolidines (2*S*,3a*S*)-**23a** and (2*R*,3a*S*)-**23c** (500 mg, 1.61 mmol, 46 %), and a mixture containing all three isomers **23a**–**23c** (300 mg, 0.97 mmol, 28 %). With the aim of complete characterization of new compounds, the sample containing **23a** and **23c** was subjected to preparative TLC (dichloromethane/EtOAc, 95:5) to give the remaining pure isomers **23a** and **23c**. **Data for (2*S*,3a*S*)-23a:** Colourless foam. R_f = 0.52 (dichloromethane/EtOAc, 4:1). $[\alpha]_D^{25}$ = +103.57 (*c* = 1.02, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 2989, 2937, 1377, 1265, 1207, 1158, 1058, 1030, 978, 853 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.95 (pseudo t, *J* = 6.6 Hz, 1 H, 5-H), 4.81 (tdd, *J* = 9.0, 3.2, 0.8 Hz, 1 H, 2-H), 4.52 (dd, *J* = 6.8, 3.8 Hz, 1 H, 4-H), 4.44 (dt, *J* = 8.3, 5.6 Hz, 1 H, 4′-H), 4.16 (dd, *J* = 8.7, 5.9 Hz, 1 H, 5′^{a}-H), 4.07 (dd, *J* = 8.7, 5.3 Hz, 1 H, 5′^{b}-H), 3.88 (ddd, *J* = 8.3, 3.7, 2.1 Hz, 1 H, 3a-H), 3.39–3.33 (m, 1 H, 6-H), 2.92 (ddd, *J* = 13.3, 8.3, 3.2 Hz, 1 H, 3^a-H), 2.74 (ddd, *J* = 13.3, 8.9, 2.1 Hz, 1 H, 3^b-H), 1.53 (s, 3 H, Me), 1.48 (s, 3 H, Me), 1.40 (s, 3 H, Me), 1.32 (s, 3 H, Me) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 118.5 (CN), 115.3 (*C*Me$_2$), 110.0 (*C*Me$_2$), 88.5 (C-4), 84.7 (C-5), 74.9 (C-4′), 74.5 (C-6), 70.0 (C-3a), 67.8 (C-5′), 64.4 (C-2), 40.0 (C-3), 27.3 (Me), 26.9 (Me), 25.6 (Me), 24.9 (Me) ppm. HRMS (ESI): calcd. for $C_{15}H_{23}N_2O_5$ [M + H]$^+$ 311.1607; found 311.1600. **Data for (2*R*,3a*R*)-23b:** Colourless oil. R_f = 0.60 (cyclohexane/EtOAc, 3:7). $[\alpha]_D^{25}$ = –83.67 (*c* = 1.00, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 2985, 2937, 1372, 1259, 1206, 1159, 1073, 1055, 1008, 847 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.86 (dd, *J* = 6.3, 0.9 Hz, 1 H, 5-H), 4.75 (dd, *J* = 9.1, 4.2 Hz, 1 H, 2-H), 4.61 (pseudo t, *J* = 5.9, 5.7 Hz, 1 H, 4-H), 4.22 (ddd, *J* = 7.0, 6.1, 4.2 Hz, 1 H, 4′-H), 4.15 (dd, *J* = 8.5, 7.2 Hz, 1 H, 5′^{a}-H), 3.93–3.90 (m, 1 H, 3a-H), 3.87 (dd, *J* = 8.6, 6.1 Hz, 1 H, 5′^{b}-H), 3.75 (d, *J* = 4.1 Hz, 1 H, 6-H), 3.04 (ddd, *J* = 12.4, 9.1, 1.6 Hz, 1 H, 3^b-H), 2.71 (ddd, *J* = 12.6, 8.4, 4.2 Hz, 1 H, 3^a-H), 1.43 (s, 3 H, Me), 1.42 (s, 3 H, Me), 1.31 (s, 3 H, Me), 1.30 (s, 3 H, Me) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 119.3 (CN), 112.9 (*C*Me$_2$), 109.9 (*C*Me$_2$), 83.8 (C-5), 82.5 (C-4), 74.9 (C-4′), 73.0 (C-6), 67.8 (C-3a), 67.2 (C-5′), 64.4 (C-2), 35.9 (C-3), 26.5 (Me), 26.4 (Me), 24.5 (Me), 24.0 (Me) ppm. HRMS (ESI): calcd. for $C_{15}H_{23}N_2O_5$ [M + H]$^+$ 311.1607; found 311.1600. **Data for (2*R*,3a*S*)-23c:** Colourless solid. R_f = 0.42 (dichloromethane/EtOAc, 4:1). M.p. 154–155 °C. $[\alpha]_D^{25}$ = +117.17 (*c* = 1.02, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 2978, 2929, 1371, 1262, 1207, 1154, 1064, 1036, 995, 846 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.03 (pseudo t, *J* = 6.5 Hz, 1 H, 5-H), 4.75 (dd, *J* = 6.8, 3.7 Hz, 1 H, 4-H), 4.56 (dd, *J* = 9.1, 5.5 Hz, 1 H, 2-H), 4.46 (ddd, *J* = 8.7, 5.8, 5.2 Hz, 1 H, 4′-H), 4.13 (dd, *J* = 8.6, 6.0 Hz, 1 H, 5′^{a}-H), 3.99 (dd, *J* = 8.6, 5.2 Hz, 1 H, 5′^{b}-H), 3.84 (ddd, *J* = 7.7, 3.8, 1.7 Hz, 1 H, 3a-H), 3.31 (dd, *J* = 8.7, 6.4 Hz, 1 H, 6-H), 2.96 (ddd, *J* = 13.0, 9.1, 7.7 Hz, 1 H, 3^b-H), 2.69 (ddd, *J* = 13.0, 5.5, 1.7 Hz, 1 H, 3^a-H), 1.53 (s, 3 H, Me), 1.48 (s, 3 H, Me), 1.39 (s, 3 H, Me), 1.36 (s, 3 H, Me) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 116.9 (CN), 115.3 (*C*Me$_2$), 110.0 (*C*Me$_2$), 87.6 (C-4), 84.9 (C-5), 75.2 (C-6), 74.9 (C-4′), 71.3 (C-3a), 67.8 (C-5′), 63.8 (C-2), 39.2 (C-3), 27.2 (Me), 26.9 (Me), 25.5 (Me), 24.8 (Me) ppm. HRMS (ESI): calcd. for $C_{15}H_{23}N_2O_5$ [M + H]$^+$ 311.1607; found 311.1599.

(2*S*,3*R*,3a*R*,4*R*,5*S*,6*S*)-6-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-4,5-isopropylidenedioxyhexahydropyrrolo[1,2-*b*]isoxazol-2,3-diyl Carbonate (24): Nitrone **1** (300 mg, 1.17 mmol) was placed into the reaction flask, followed by toluene (12 mL) and vinylene carbonate (**8**; 455 mg, 5.29 mmol). The flask was sealed, and the mixture was stirred at 100 °C for 3 d. After this time, TLC showed that the reaction was complete (hexanes/EtOAc, 1:4). The mixture was concentrated in vacuo, and the residue was purified by FCC (hexanes/EtOAc, 6:4) to give one pure isoxazolidine **24** (360 mg, 1.05 mmol, 90 %) as a colourless solid. R_f = 0.29 (cyclohexane/EtOAc, 6:4). M.p. 189–190 °C. $[\alpha]_D^{25}$ = +105.80 (*c* = 0.98, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 2989, 2937, 1808, 1796, 1372, 1173, 1086, 1058, 988, 863 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.01 (d, *J* = 5.2 Hz, 1 H, 2-H), 5.58 (d, *J* = 5.2 Hz, 1 H, 3-H), 4.97 (d, *J* = 6.2 Hz, 1 H, 5-H), 4.88 (pseudo t, *J* = 5.9, 5.6 Hz, 1 H, 4-H), 4.22 (td, *J* = 7.6, 7.3, 2.3 Hz, 1 H, 4′-H), 4.06–4.02 (m, 3 H, 5′^{a}-H, 5′^{b}-H, 3a-H), 3.92–3.91 (m, 1 H, 6-H), 1.42 (s, 3 H, Me), 1.33 (s, 3 H, Me), 1.32 (s, 3 H, Me), 1.29 (s, 3 H, Me) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 153.1 (C=O), 113.4 (*C*Me$_2$), 109.7 (*C*Me$_2$), 101.0 (C-2), 87.1 (C-5), 84.9 (C-3), 81.6 (C-4), 76.1 (C-4′), 74.5 (C-3a), 71.0 (C-6), 66.2 (C-5′), 26.1 (Me), 25.8 (Me), 25.7 (Me), 23.7 (Me) ppm. HRMS (ESI): calcd. for $C_{15}H_{22}NO_8$ [M + H]$^+$ 344.1340; found 344.1340.

(4*S*,5*R*,6*R*)-6-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-4,5-isopropylidenedioxyhexahydropyrrolo[1,2-*b*]isoxazol-2,3-diyl Carbonate (25): Nitrone **4** (300 mg, 1.17 mmol) was placed into a reaction flask, followed by toluene (12 mL) and vinylene carbonate (**8**; 250 mg, 2.91 mmol). The flask was sealed, and the mixture was stirred at 100 °C for 24 h, after which time TLC showed that the reaction was complete (hexanes/EtOAc, 1:4). The solvent was then

evaporated to dryness, and the residue was purified by FCC (hexanes/EtOAc, 6:4) to give two pure isoxazolidines (2*S*,3*R*,3a*R*)-**25a** (265 mg, 0.77 mmol, 66 %) and (2*R*,3*S*,3a*S*)-**25b** (40 mg, 0.12 mmol, 10 %). **Data for (2*S*,3*R*,3a*R*)-25a:** Colourless solid. R_f = 0.25 (cyclohexane/EtOAc, 6:4). M.p. 152–153 °C. $[\alpha]_D^{25}$ = +112.10 (*c* = 1.03, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 2985, 2939, 1793, 1776, 1374, 1179, 1156, 1055, 1013, 981, 850 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 6.11 (dd, *J* = 5.1, 1.8 Hz, 1 H, 2-H), 5.48 (d, *J* = 5.1 Hz, 1 H, 3-H), 4.96 (pseudo t, *J* = 6.7, 6.4 Hz, 1 H, 5-H), 4.61 (dd, *J* = 7.0, 5.0 Hz, 1 H, 4-H), 4.43 (ddd, *J* = 8.6, 5.8, 5.0 Hz, 1 H, 4′-H), 4.15 (dd, *J* = 8.8, 5.9 Hz, 1 H, 5′^{a}-H), 4.06 (dd, *J* = 8.8, 4.9 Hz, 1 H, 5′^{b}-H), 3.90 (d, *J* = 5.0 Hz, 1 H, 3a-H), 3.41 (ddd, *J* = 8.7, 6.1, 1.8 Hz, 1 H, 6-H), 1.54 (s, 3 H, Me), 1.48 (s, 3 H, Me), 1.39 (s, 3 H, Me), 1.34 (s, 3 H, Me) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 152.5 (C=O), 116.4 (*C*Me_2), 110.1 (*C*Me_2), 99.9 (C-2), 85.2 (C-3), 84.4 (C-5), 82.8 (C-4), 75.9 (C-3a), 75.1 (C-6), 74.7 (C-4′), 67.7 (C-5′), 27.1 (Me), 26.9 (Me), 25.6 (Me), 24.7 (Me) ppm. HRMS (ESI): calcd. for $C_{15}H_{22}NO_8$ $[M + H]^+$ 344.1340; found 344.1339. **Data for (2*R*,3*S*,3a*S*)-25b:** Colourless syrup. R_f = 0.42 (cyclohexane/EtOAc, 6:4). $[\alpha]_D^{25}$ = –103.20 (*c* = 1.00, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 2987, 2939, 1809, 1373, 1206, 1162, 1059, 989, 863, 723 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 6.02 (d, *J* = 5.2 Hz, 1 H, 2-H), 5.58 (d, *J* = 5.2 Hz, 1 H, 3-H), 4.91 (d, *J* = 6.3 Hz, 1 H, 5-H), 4.80 (pseudo t, *J* = 6.0, 5.5 Hz, 1 H, 4-H), 4.23 (ddd, *J* = 7.3, 6.0, 3.2 Hz, 1 H, 4′-H), 4.16 (dd, *J* = 8.8, 7.4 Hz, 1 H, 5′^{a}-H), 4.01 (d, *J* = 5.3 Hz, 1 H, 3a-H), 3.90 (d, *J* = 3.2 Hz, 1 H, 6-H), 3.85 (dd, *J* = 8.8, 6.0 Hz, 1 H, 5′^{b}-H), 1.42 (s, 3 H, Me), 1.41 (s, 3 H, Me), 1.30 (s, 3 H, Me), 1.29 (s, 3 H, Me) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 153.1 (C=O), 113.2 (*C*Me_2), 110.1 (*C*Me_2), 101.3 (C-2), 84.7 (C-3), 83.8 (C-5), 81.9 (C-4), 74.4 (C-4′), 73.5 (C-6), 73.4 (C-3a), 67.0 (C-5′), 26.3 (Me), 26.1 (Me), 24.2 (Me), 23.6 (Me) ppm. HRMS (ESI): calcd. for $C_{15}H_{22}NO_8$ $[M + H]^+$ 344.1340; found 344.1340.

Crystallography: Data collection and cell refinement for **1** were carried out using a Stoe StadiVari Eulerian cradle diffractometer with a Pilatus 300K HPAD detector (hybrid pixel array detector) at 100 K, using Cu-K_α radiation (λ = 1.54186 Å, microfocus source Xenocs FOX3D) for the measurement. The intensity data for **4**, **18b**, and **21a** were collected with a Rigaku XtaLAB diffractometer with an AFC11 partial χ geometry goniometer, equipped with a Saturn 724+ HG CCD detector at 120 K. Mo-K_α radiation (λ = 0.71075 Å) or Cu-K_α radiation (1.54186 Å), MicroMax-007HF DW rotating anode source, multilayer optic VariMax DW, was used for the measurement. The diffraction intensities were corrected for Lorentz, polarization, and absorption effects. The structure was solved by direct or charge-flipping methods using SHELXT,[16] SIR-2011,[17] or SuperFlip,[18] and was refined by a full-matrix least-squares procedure with the SHELXL (ver. 2016/4),[19] or Olex2.refine,[20] and drawn with the OLEX2 package.[21] The crystal structures of **1** and **21a** contain two and eight, respectively, crystallographically independent molecules (see the Supporting Information). The chirality of the carbon atoms was confirmed by using the PLATON program.[22] CCDC 1499614 (for **1**), 1499615 (for **4**), 1499616 [for **18b** (Cu)], 1499617 [for **18b** (Mo)], and 1499618 (for **21a**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre. **Crystal Data for 1:** $C_{12}H_{19}NO_5$ (*M* = 257.28 g/mol): monoclinic, space group $P2_1$ (No. 4), *a* = 60323(2) Å, *b* = 10.1048(3) Å, *c* = 21.2121(8) Å, β = 90.061(3)°, *V* = 1292.99(8) Å^3, *Z* = 4, *T* = 100 K, μ(Cu-K_α) = 0.861 mm^{-1}, $D_{calcd.}$ = 1.322 g/cm^3, 75031 reflections measured (4.17° ≤ 2Θ ≤ 143.08°), 3979 unique (R_{int} = 0.0306, R_{sigma} = 0.0180), which were used in all calculations. The final R_1 was 0.0269 [$I > 2\sigma(I)$], and wR_2 was 0.0663 (all data). Chirality of the carbon atoms: C-1 (*S*), C-2 (*S*), C-3 (*R*), C-5 (*S*). **Crystal Data for 4:** $C_{12}H_{19}NO_5$ (*M* = 257.28 g/mol): orthorhombic, space group $P2_12_12_1$ (No. 19), *a* = 8.9686(6) Å, *b* = 10.4636(7) Å, *c* = 13.7884(11) Å, *V* = 1293.96(16) Å^3, *Z* = 4, *T* = 120 K, μ(Cu-K_α) = 0.861 mm^{-1}, $D_{calcd.}$ = 1.321 g/cm^3, 10691 reflections measured (10.62° ≤ 2Θ ≤ 133.90°), 2262 unique (R_{int} = 0.0274, R_{sigma} = 0.0141) which were used in all calculations. The final R_1 was 0.0339 [$I > 2\sigma(I)$], and wR_2 was 0.0884 (all data). Chirality of the carbon atoms: C-1 (*R*), C-2 (*R*), C-3 (*S*), C-5 (*S*). **Crystal Data for 18b (Cu):** $C_{22}H_{29}NO_7$ (*M* = 419.46 g/mol): orthorhombic, space group $P2_12_12_1$ (No. 19), *a* = 10.2363(7) Å, *b* = 10.4683(7) Å, *c* = 20.1860(14) Å, *V* = 2163.1(3) Å^3, *Z* = 4, *T* = 120 K, μ(Cu-K_α) = 0.795 mm^{-1}, $D_{calcd.}$ = 1.288 g/cm^3, 8988 reflections measured (19.04° ≤ 2Θ ≤ 130.60°), 3198 unique (R_{int} = 0.0338, R_{sigma} = 0.0192), which were used in all calculations. The final R_1 was 0.0426 [$I > 2\sigma(I)$] and wR_2 was 0.1152 (all data). Chirality of the carbon atoms: C-1 (*S*), C-3 (*S*), C-4 (*R*), C-5 (*S*), C-6 (*S*), C-7 (*S*). **Crystal Data for 18b (Mo):** $C_{22}H_{29}NO_7$ (*M* = 419.46 g/mol): orthorhombic, space group $P2_12_12_1$ (No. 19), *a* = 10.2308(10) Å, *b* = 10.4653(10) Å, *c* = 20.121(2) Å, *V* = 2154.3(4) Å^3, *Z* = 4, *T* = 120 K, μ(Mo-K_α) = 0.096 mm^{-1}, $D_{calcd.}$ = 1.293 g/cm^3, 11218 reflections measured (4.46° ≤ 2Θ ≤ 52.54°), 4331 unique (R_{int} = 0.0124, R_{sigma} = 0.0143), which were used in all calculations. The final R_1 was 0.0280 [$I > 2\sigma(I)$] and wR_2 was 0.0720 (all data). Chirality of the carbon atoms: C-1 (*S*), C-3 (*S*), C-4 (*R*), C-5 (*S*), C-6 (*S*), C-7 (*S*). **Crystal Data for 21a:** $C_{22}H_{19}NO_5$ (*M* = 419.46 g/mol): monoclinic, space group $P2_1$ (No. 4), *a* = 28.413(2) Å, *b* = 10.4741(7) Å, *c* = 28.792(2) Å, β = 97.966(1)°, *V* = 8485.9(10) Å^3, *Z* = 16, *T* = 120 K, μ(Mo-K_α) = 0.098 mm^{-1}, $D_{calcd.}$ = 1.313 g/cm^3, 112965 reflections measured (2.85° ≤ 2Θ ≤ 52.00°), 33133 unique (R_{int} = 0.0385, R_{sigma} = 0.0329) which were used in all calculations. The final R_1 was 0.0488 [$I > 2\sigma(I)$] and wR_2 was 0.1419 (all data). Chirality of the carbon atoms: C-1 (*S*), C-3 (*S*), C-4 (*S*), C-5 (*R*), C-6 (*R*), C-7 (*S*).

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